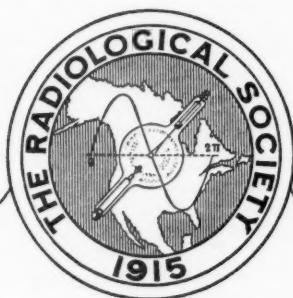


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RADIOLOGY

A MONTHLY JOURNAL DEVOTED
TO CLINICAL RADIOLOGY AND
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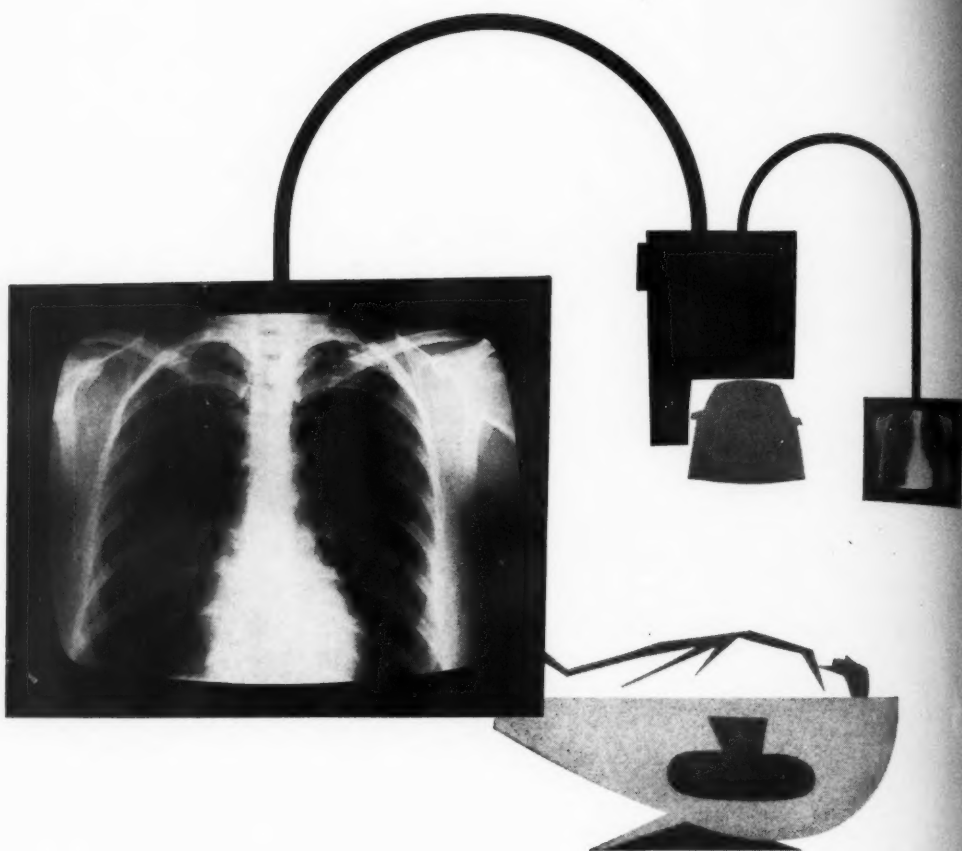
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No. 2

The Combined Radiologic and Gastroscopic Evaluation of Gastric Ulceration¹

GERALD D. DODD, M.D., and ROBERT S. NELSON, M.D.

THE OPINION that all gastric ulcers should be treated by some form of gastric resection is widely held. This is based primarily upon doubt as to the ability of the internist, radiologist, or endoscopist to differentiate the benign from the malignant ulcer and secondarily upon the belief that the operative mortality and postoperative morbidity of gastric resection are outweighed by the number of cured patients. It has been our experience that the information gained from a combination of the roentgenologic and gastroscopic methods of examination provides reliable evidence as to the presence and type of ulceration. Since it is debatable whether a patient with benign, uncomplicated disease will routinely benefit by having all or part of his stomach removed, it seems reasonable to us that clinical evaluation of the ulcer be employed to separate the candidate for immediate surgery from one who may exhibit a beneficial and lasting response to medical therapy.

As noted by others (2, 3, 14, 19, 20, 21, 22, 24, 25, 26), the relationship between the roentgenologic and gastroscopic methods of examination may be described as supplementary or complementary. In no sense are they competitive. In certain portions

of the stomach there is excellent correlation between the two; other areas and entities may be difficult to evaluate by either method alone. It is our purpose to illustrate again the advantage of combining these procedures. In so doing, we wish to emphasize the use of intragastric color photography as a method of permanently recording the findings of the gastroscopist. Much of the criticism of gastroscopy has been based upon lack of documentation of the observations. It is frequently implied that the gastroscopist's conclusions have been influenced by the preceding roentgenologic examination and cannot be regarded as an independent evaluation. The majority of the patients in this series have had endoscopic photographs and the final gastroscopic opinion has been based upon direct observation combined with an analysis of the photographs. Gastroscopy frequently has preceded the roentgenologic examination, and occasionally re-examination by the radiologist has been necessary to attempt demonstration of a lesion not appreciated originally.

For the purpose of this study, 100 patients with gastric ulceration were chosen from those seen since the introduction of intragastric color photography at the M. D. Anderson Hospital (Houston, Texas)

¹ From the Sections of Diagnostic Radiology and Gastroenterology, The University of Texas M. D. Anderson Hospital and Tumor Institute, Texas Medical Center, Houston, Texas. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

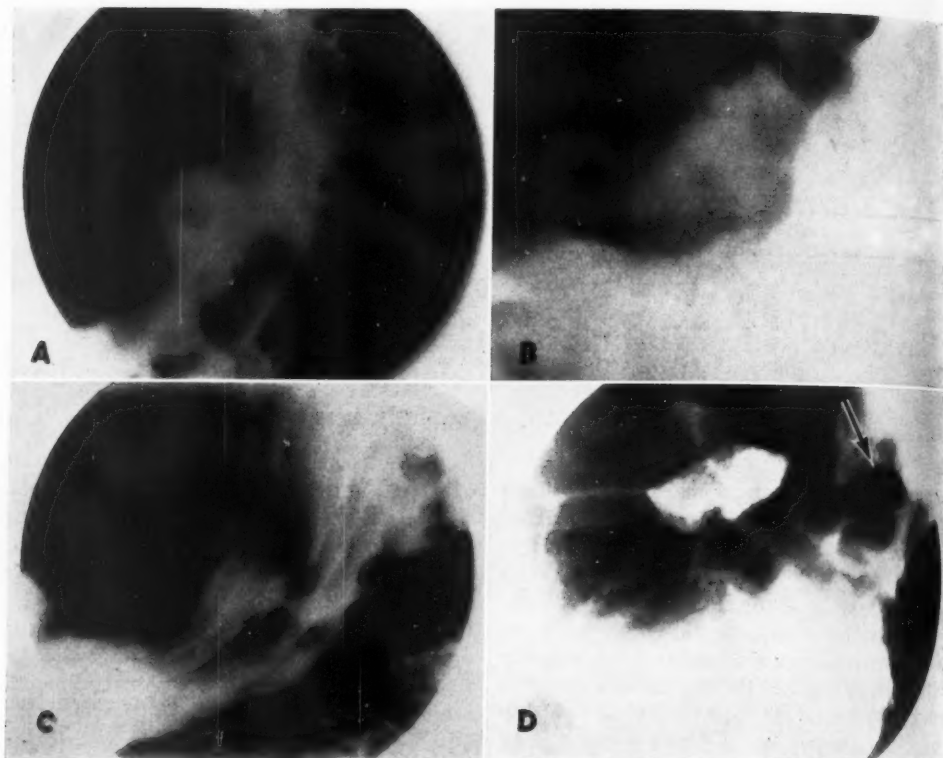


Fig. 1. Malignant ulcers. A. Ulcer within mass. There are marked distortion and infiltration of the surrounding mucosa. B. Meniscus complex of Carman and Kirklin. Note nodular characteristics of tumor cuff about crater. C. Tumor nodules partially surrounding base of shallow ulcer. Location at angulus prevented gastroscopic visualization. D. Ulceration with apparent ulcer collar and undermining. Mucosa seemingly intact save for superior margin of collar and distorted and thickened adjacent fold (arrow). The true meniscus complex is an uncommon but reliable sign.

in October 1957. Among factors determining selection were examination or attempted examination by both methods and exclusion of cases in which mass was the predominant finding. In each instance the initial radiologic and gastroscopic diagnoses were tabulated for analytical purposes. The relatively high incidence of malignant ulcers is attributable to the fact that the institution in which these examinations were done is limited to patients with proved or suspected neoplastic disease.

DIAGNOSTIC CRITERIA

Röntgenologic Criteria

The concepts of location, size, configuration, and depth of an ulcer crater have not

proved reliable in the differential diagnosis of benignity and malignancy (9, 23). Although Comfort and his associates (6) have recently re-asserted some validity for a few of these criteria, the statistical differences upon which their conclusions are based are not sufficiently great to warrant use in the individual case. Consideration of age, sex, the presence of free acid, etc., have no place in the objective analysis of roentgen findings. In our opinion the following criteria are the most reliable:

A. Ulcers of Malignant Origin: 1. The only valid sign of malignant ulceration is the demonstration of tumor in the vicinity of the crater. This may vary from unmistakable ulcer within mass (Fig. 1, A)

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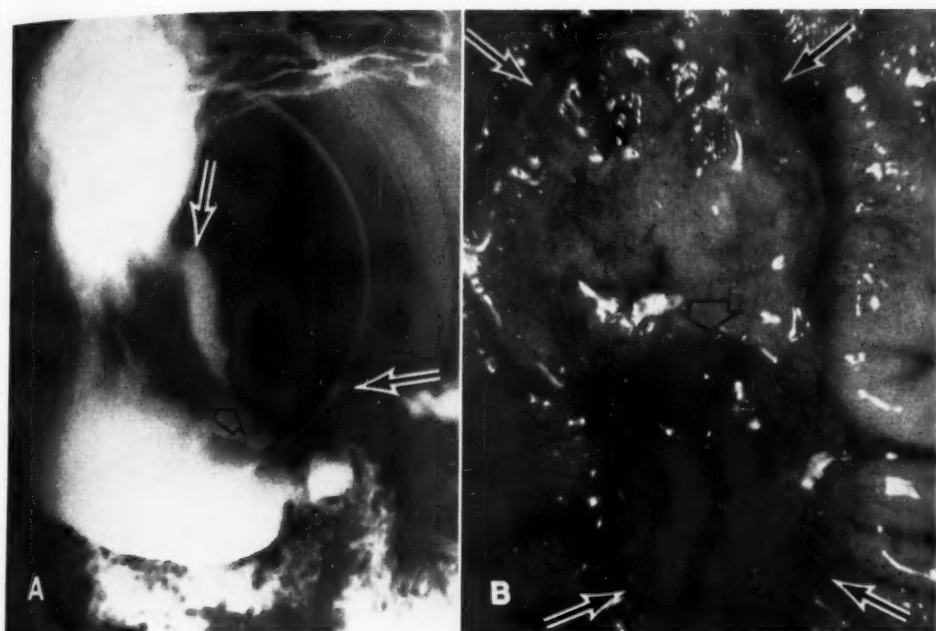


Fig. 2. Nodularity of base of ulcer. A. Huge lesser curve ulcer extending from mid pars media to pylorus (marginal arrows). Central nodule (central arrows) led to roentgen diagnosis of a malignant lesion. Histologic examination revealed large benign ulcer with central nodule of granulation tissue. Nodularity of the ulcer base is not a reliable sign of malignant disease roentgenologically and is of variable significance gastroscopically.

to interruption or distortion of the mucosal folds on a limited segment of the crater periphery. The meniscus complex of Carman and Kirklin² is the classic example of the former and pathognomonic of malignancy (Fig. 1, B). Less sharply circumscribed tumors are more commonplace, however, and evidence of neoplastic disease may be confined to small nodules about the ulcer margins (Figs. 1, C and D). Nodulation of the base of an ulcer is unreliable, since blood clots, food particles, and granulation tissue may be indistinguishable from tumor nodules (Fig. 2).

Minimal changes in the peripheral mucosa must be regarded with caution, since they may be indistinguishable from inflammatory infiltration. Mucosal destruction must be unequivocal and should be regarded as a function of mass rather than a separate criterion of malignant disease.

B. Benign Ulcers: The following criteria are valid only in the absence of mass or in those cases in which the presence of tumor is equivocal. In the latter instance their demonstration would tend to place the ulcer in the benign category.

1. *Hampton's Sign:* When present, Hampton's sign is probably the most reliable radiologic sign of benign gastric ulceration. We have been told that Hampton ascribed approximately 98 per cent accuracy to this finding, although no figures were published as to this point by Shumacher and Hampton (28). Wolf and Marshak (33) noted it in but one instance of malignant ulceration, and it was unquestionably present in one malignant ulcer in our series. The sign consists of a radiolucent line, seldom more than 1 mm. in width, which may partially or completely traverse the orifice of an ulcer (Fig. 3, A). Its visualization requires a true profile view of the crater, and high-kilovoltage films are of value in its demonstration. Compression studies are useful

² This sign has been widely misunderstood and for additional information the reader is referred to the recent lucid description of its components by Wolf and Sherkow (34).

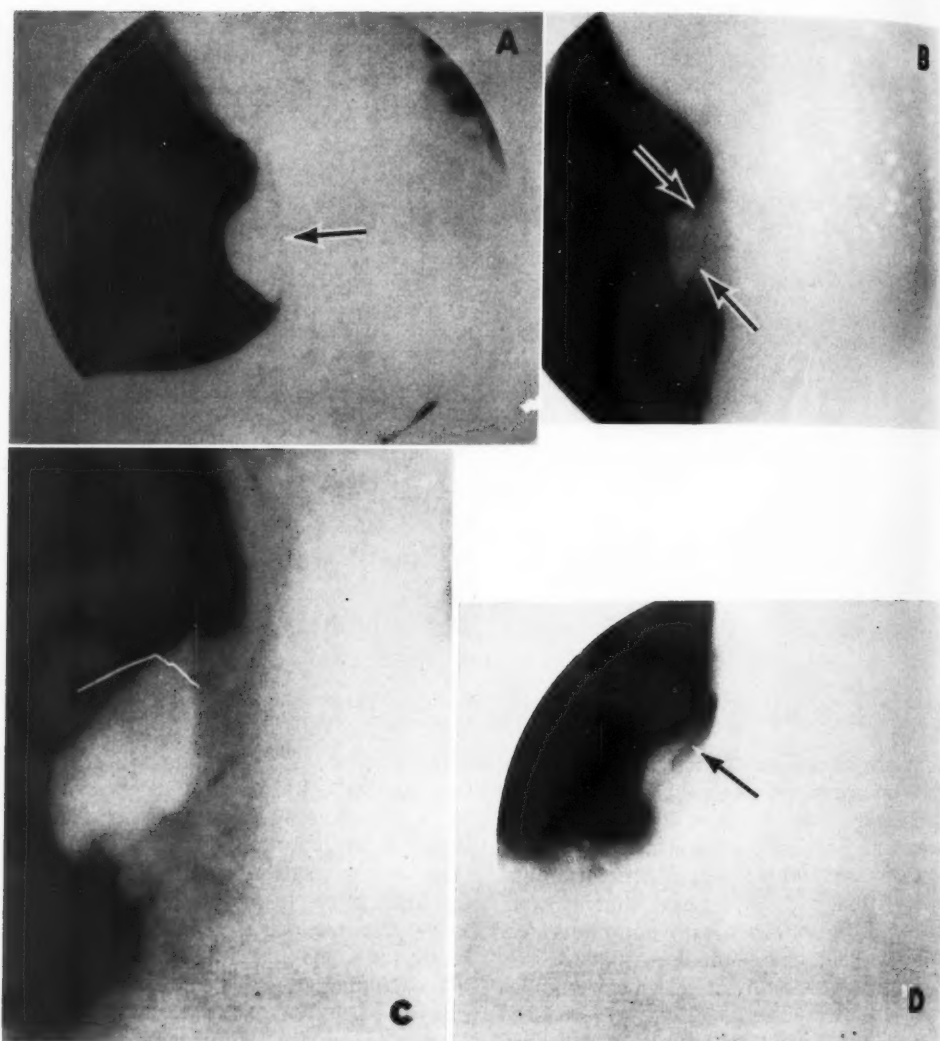


Fig. 3. Hampton's line. A. Complete traversal of the ulcer orifice by a 1-mm. line representative of the thin undermined mucosa in profile.

B. Double lines resulting from slight obliquity of projection.

C and D. Large lesser curve ulcer with collar. Hampton's line apparent after three weeks of therapy.

only in displacing portions of the stomach so that the profile projection may be obtained. The line may be seen at only one edge of the crater (Fig. 4, D), or may be present as a double band when a slight deviation from the true profile view is obtained (Fig. 3, B). Shumacher and Hampton have conclusively shown that the radiolucency is due to the thin, undermined marginal mucosa of the crater.

Unfortunately the line cannot be demonstrated in every case, and its absence is not of diagnostic significance, since it may become evident only with healing of an ulcer (Figs. 3, C and D) or may never be seen in an obviously benign crater which undergoes complete resolution. The tendency of an ulcer to heal eccentrically is possibly the explanation for the several forms in which the line is seen.

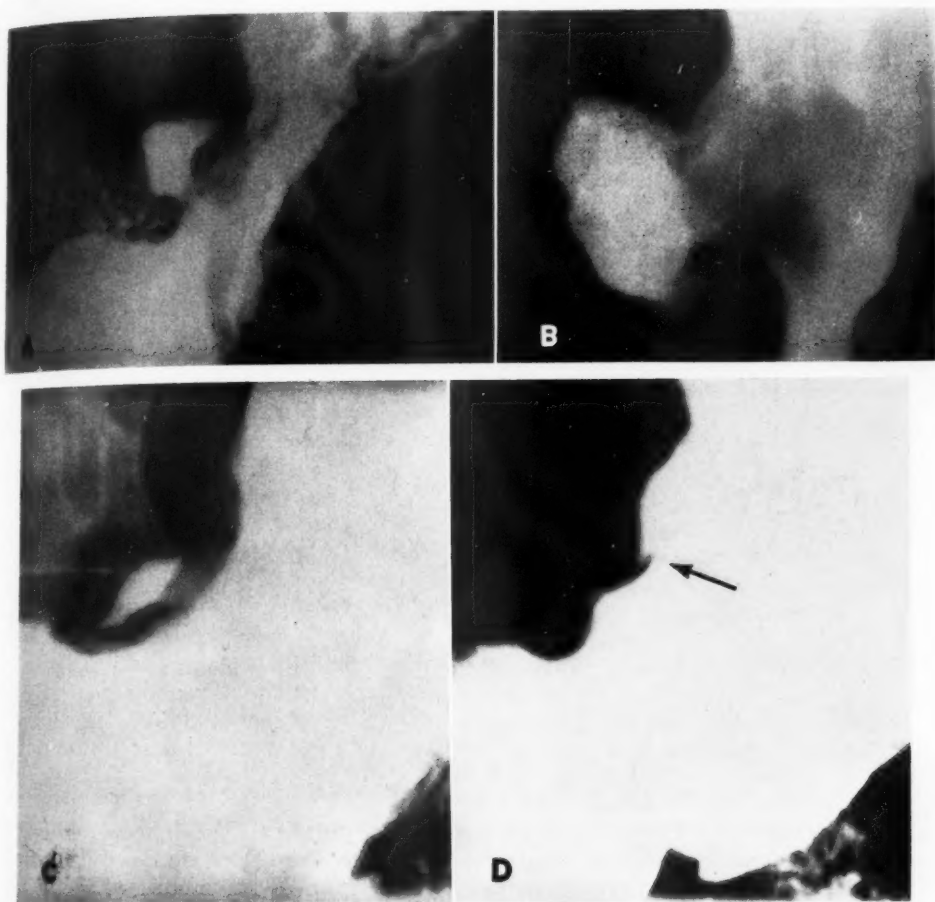


Fig. 4. Ulcer collar and ulcer mound. A. Typical ulcer collar resulting from heaping of mobile mucosa about mouth of ulcer.

B. Large collar with penetrating ulcer. The size of the collar varies greatly in the individual case.

C and D. Ulcer mound simulating meniscus complex (compression study). Without compression, partial Hampton's line seen (arrow). (Courtesy Drs. J. Martin and L. Lemak, Houston, Texas).

2. *The Ulcer Collar:* This apt description has been applied by Wolf and Marshak to the relatively translucent band which may intervene between the niche and the lumen of the stomach (Figs. 3, C; 4, A and B; 6, B). These investigators do not agree with Shumacher and Hampton that this is a projection of Hampton's line when seen tangentially, since both may be present simultaneously (Figs. 4, C and D). Rather, they regard the collar as a manifestation of limited distensibility of the gastric wall immediately surrounding the niche and postulate

that it may result from an inflammatory exudate about the crater, with perhaps some local spastic element.

In this respect, it is interesting to note Barclay's explanation (1) for the disparity between an ulcer which radiographically appears to penetrate the gastric wall and the subsequent surgical specimen which shows a flat crater that may barely reach the muscular coat and shows no significant undermining. It is his conclusion, in keeping with the theories of Forsell (10) and Berg (4), that in "conscious life" the mucous membrane forms a protective

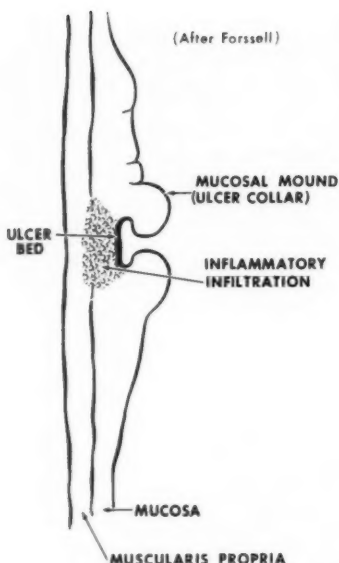


Fig. 5 Schematic representation of anatomic basis for ulcer collar and ulcer mound.

mound about the ulcerated surface and thus produces a relatively deep pocket (Fig. 5). Since movements of the mucous membrane are controlled by the muscularis mucosae, the findings may be absent in the resected stomach unless submucosal scarring has developed. Fluctuations in the distribution of the submucosal fluid also play a part but are difficult to demonstrate in the surgical specimen. Wolf and Marshak stress the fact that the appearance of the collar does not suggest complete rigidity and that it is smooth as contrasted with rolled edge of the tumor seen in the meniscus sign. They regard the ulcer collar and Hampton's line as of similar significance. The reader is referred to their comprehensive description of the roentgenologic characteristics of benign gastric ulceration for additional details.

3. *Intact Mucosa* (Fig. 6): The value of the demonstration of intact mucosa about the margins of an ulcer has been emphasized by Kirsh (15) and others, but is disputed by Lloyd *et al.* (16), who considered it possible, in over one-third of their 26 cases of carcinoma in which there was a delay in diagnosis, to demonstrate con-

verging rugae. In some of their roentgenograms, however, it appears that the barium is actually trapped between ridges of tumor rather than normal folds (Fig. 10; D in color plate). In other illustrations listed as showing fold convergence, the mucosa is apparent on only one aspect of the crater, a finding which has previously been described as suggestive of malignant disease (11).

It should be noted that the "ulcer collar" of Wolf and Marshak produces a persistent defect which intervenes between the crater and adjacent fold pattern, but the factor of pliability is important in differentiation. Occasionally the collar may be of sufficient size to warrant the term "ulcer mound." This may occur with craters of any size and must be differentiated from mass with central ulceration (Fig. 4, C and D). Wolf and Marshak (33) point out that the surface of the ulcer mound is sharply demarcated and smooth, with intact folds over it, and that in most instances the margins join the adjacent stomach in a smooth flowing fashion, without sharp discontinuity.

Gastrosopic Criteria

The differential gastrosopic criteria of an ulcer, since they are based upon direct observation of the mucosa of the inflated stomach, are not exact counterparts of those evident radiologically. Color, form, and extent of the lesion as seen within the entire stomach play a major role in differentiation. While the form of large infiltrative lesions frequently may be demonstrated radiologically, this feature is even more apparent gastrosopically. As Schindler (25) has noted, the inspection of the living tissue through a gastroscope is superior to that of the excised specimen, although by no means infallible in differential diagnosis.

The following observations are felt to be the most important:

1. *Characteristics of the Ulcer Edge:* The sharply demarcated or "punched-out" appearance of the edge of the benign ulcer is an extremely reliable criterion of be-

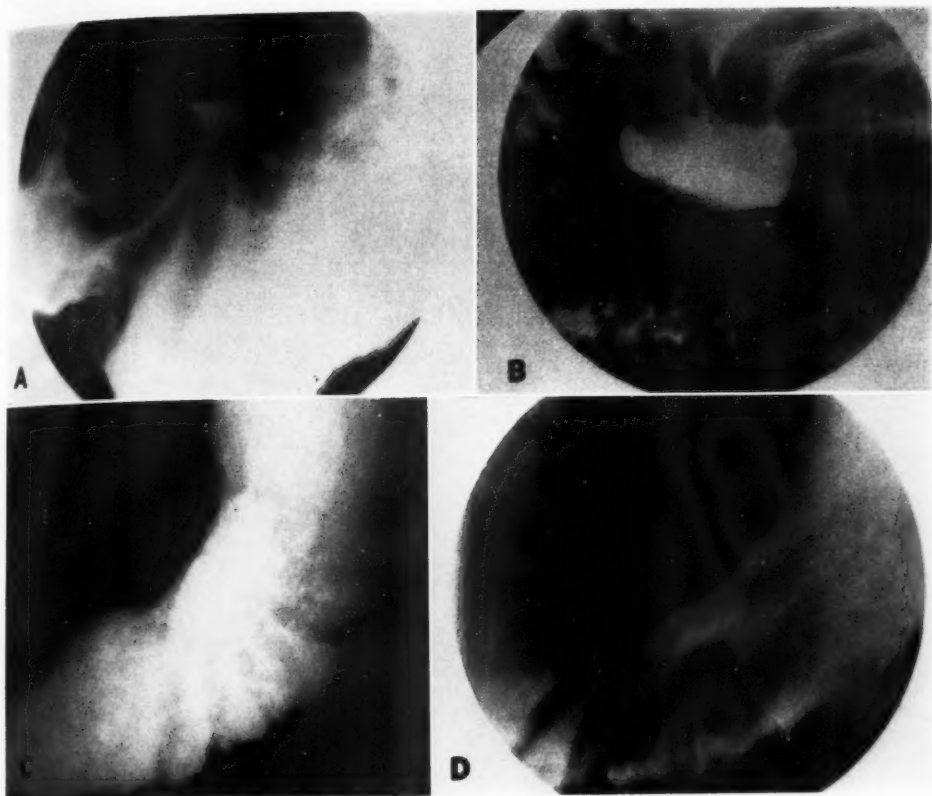


Fig. 6. Intact marginal mucosa. A. Radiating folds about benign lesser curve ulcer. B. Intact folds and ulcer collar in large benign ulcer of greater curvature of pars media. C. Apparent intraluminal mass with shallow ulcer in patient with systemic lymphosarcoma. D. Spot-pressure film of C, showing intact mucosa. Ulcer refractory to therapy. Pathology: Benign chronic superficial gastric ulcer unrelated to systemic disease.

Note that, although folds in all cases vary in width, the pattern is orderly and all extend to the ulcer margins.

nignancy (Fig. 7; A in color plate). Infiltration of an edge or necrotic shading into the surrounding tissue, even if present in one area only, is highly suggestive of malignancy. The benign ulcer may frequently have serpiginous extensions into the surrounding tissue, but the edge will remain sharply defined. We have found such extensions characteristic of numerous benign ulcerations (Fig. 8; B in color plate). Similar extensions of a malignant ulcer are accompanied by necrosis and blurring of the edge of the crater, usually in such a gross fashion that the nature of the lesion is unmistakable. Bleeding of the edge of a malignant ulcer is frequently seen but rarely occurs in the benign lesion,



Fig. 7. Benign chronic ulcer of lesser curvature with obstruction indicated by arrows. Roentgen diagnosis: Probable benign ulcer. Detail obscured by gastric residue.

See A in color plate.

GASTROSCOPIC PHOTOGRAPHS (See opposite page)

A. Benign chronic ulcer of lesser curvature with obstruction. See Fig. 7. Characteristic sharp delineation of ulcer with intact surrounding mucosa; crater filled with mucus.

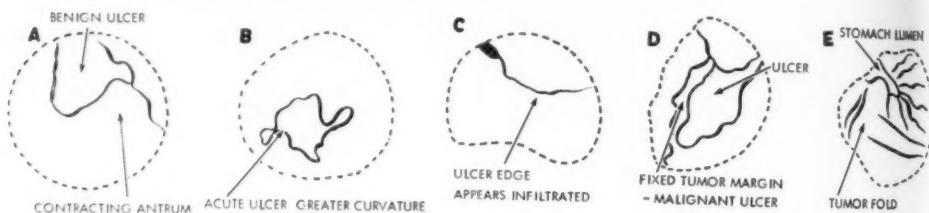
B. Benign superficial greater curvature ulcer undetected roentgenologically. See Fig. 8. Gastroscopic photographs obtained April 7, 1959. The serpiginous extensions shown in the diagram are frequently seen on gastroscopic study of benign ulcers.

C. Benign ulcer penetrating pancreas misinterpreted gastroscopically as malignant, because of infiltration of ulcer margin. See Fig. 9. The upper margin of the ulcer rim shows "undercutting," which is probably the counterpart of the ulcer collar. The identification of severe inflammatory infiltration as neoplastic is the most frequent gastroscopic error.

D. Malignant ulcer in region of incisura angularis. Excellent correlation with roentgen study (Fig. 10).

E. Malignant ulcer misinterpreted roentgenologically (Fig. 11). The gastroscopic photograph shows clear-cut tumor infiltration of the mucosa, which prevented visualization of the ulcer.

DIAGRAMMATIC REPRESENTATION OF GASTROSCOPIC PHOTOGRAPHS A-E



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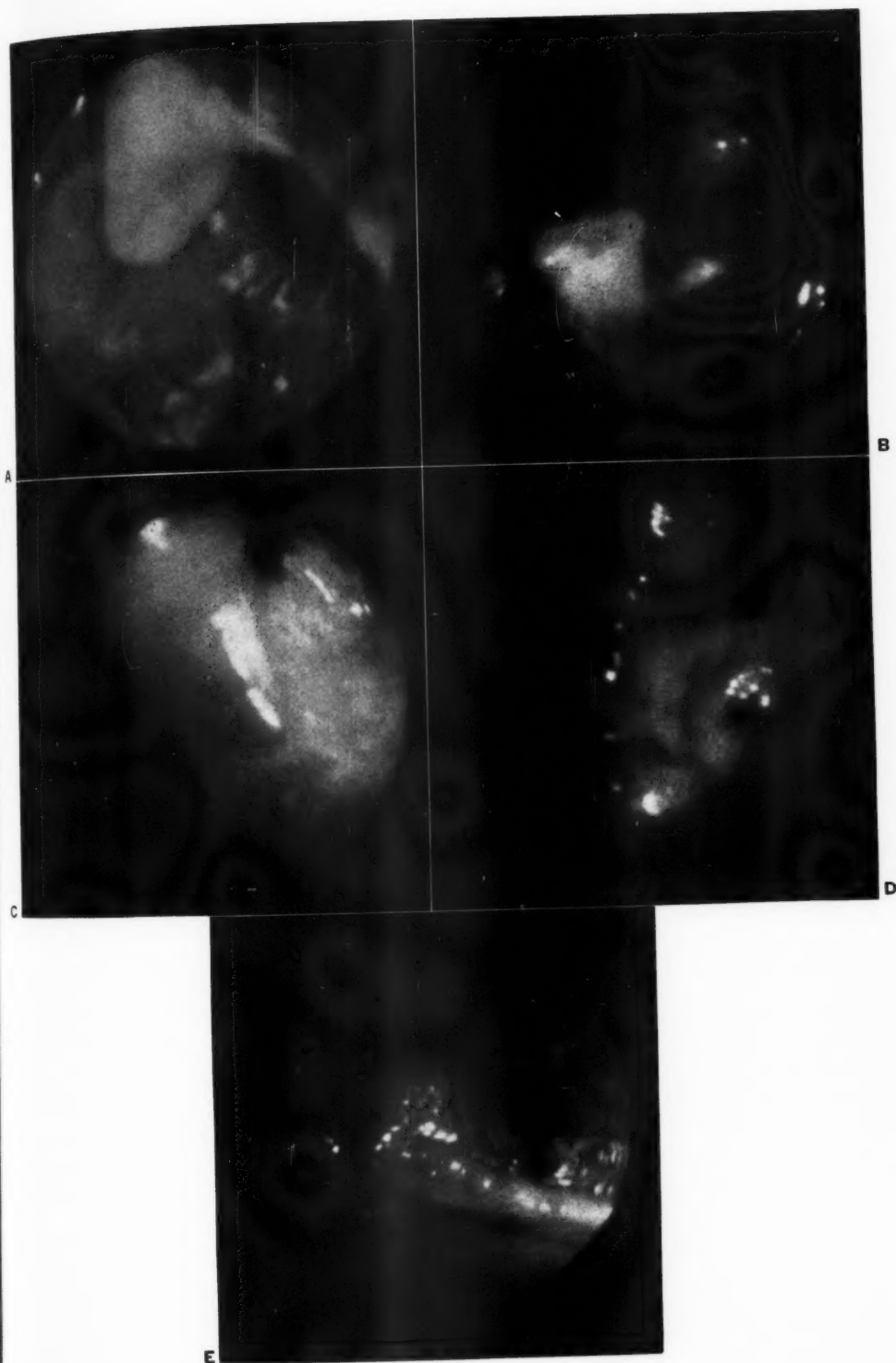




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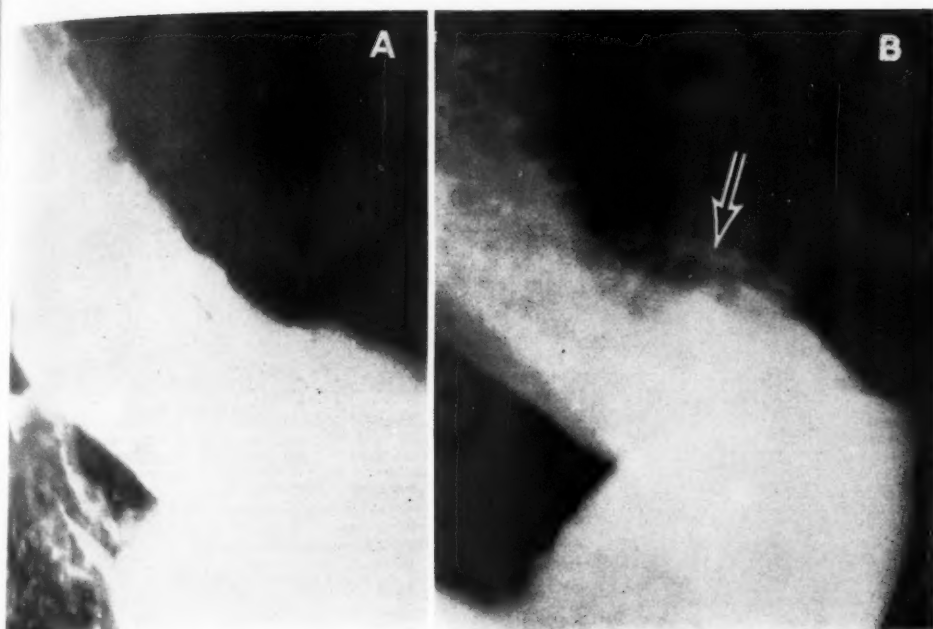


Fig. 8. Benign superficial greater curvature ulcer undetected roentgenologically. A. Upper gastrointestinal roentgenogram, March 26, 1959, interpreted as negative save for situs inversus abdominis.

B. Repeat study, April 22, 1959, also interpreted as negative. Arrows indicate probable ulcer retrospectively. See B in color plate.

although there may be bleeding in the crater of the latter. In very large benign ulcerations an apparent undercutting of the edge may be demonstrable and possibly is the gastroscopic counterpart of the ulcer collar (C in color plate). Unfortunately, in small ulcerations, the crater is frequently filled with mucus and undercutting is not recognizable.

2. *Form of the Crater:* Most ulcer craters as seen through the gastroscope are filled with mucus, a finding which interferes with depth perception. What appears to be necrosis in the crater may be simply retained food. Unequivocal tumor nodules in the base of the crater may be identified, however, and in large malignant ulcerations tissue necrosis can be unmistakable. In both instances, the diagnosis of malignancy usually can be made with certainty, although large benign ulcers which penetrate into the pancreas may give similar appearances (Fig. 9; C in color plate). In such cases the roentgen findings may be more reliable.

3. *Surrounding Mucosa and Stomach as a Whole:* Converging folds are seldom seen gastroscopically, since inflation of the stomach usually obliterates the membrane pattern. Occasionally scarring in the base of a benign ulcer may preserve fold convergence in the inflated organ, but this is not a good differential point. Tumor nodules or gross infiltration of a large area surrounding the crater are pathognomonic of malignancy (Fig. 10; D in color plate), but the interpretation of the latter feature has caused the greatest number of gastroscopic mistakes. A diagnosis of malignant disease in a very large benign ulcer, with a heavy inflammatory infiltrate thickening and stiffening the neighboring mucosa, has been our most frequent error (Fig. 9; C in color plate). In most cases, however, tumor may be unequivocally diagnosed, even when the ulcer itself cannot be seen because of the surrounding neoplastic infiltration (Fig. 11; E in color plate); the infiltrate itself remains one of the most useful criteria for malignancy. Similarly,



Fig. 9. Benign ulcer penetrating pancreas, misinterpreted gastroscopically. Roentgen study interpreted as benign penetrating ulcer. See C in color plate.

the marked mucosal inflammatory changes usually associated with benign ulceration, regardless of size, are in most instances good evidence of benignity. Mucosal atrophy is not a reliable sign of a malignant lesion; we have seen marked atrophic changes in many cases of benign ulcer, some of which have healed completely.

RESULTS

The results obtained by the combined method of examination are detailed in Tables 1A and 1B. In each instance the diagnosis has been proved by microscopic examination or long-term follow-up, including multiple gastroscopic and roentgenologic examinations. The most significant statistic is an accuracy of 95 per cent with the use of both procedures as compared to 81 and 83 per cent respectively for the gastroscopic and roentgenologic examinations alone. Although only 3 lesions were incorrectly interpreted by both methods (97 per cent overall accuracy), 2 additional cases correctly interpreted roentgenologically as benign ul-

TABLE 1A: COMPARISON OF INITIAL ROENTGENOLOGIC AND GASTROSCOPIC EXAMINATIONS IN 100 GASTRIC ULCERS

	Benign Gastric Ulcers	Malignant Gastric Ulcers	Total Cases
Concurring diagnoses	52 (67.5%)	15 (65.2%)	67 (67%)
X-ray correct; gastroscopy incorrect*	15 (19.5%)	1 (4.4%)	16 (16%)
Gastroscopy correct; x-ray incorrect*	9 (11.7%)	5 (21.7%)	14 (14%)
Both incorrect	1 (1.3%)	2 (8.7%)	3 (3%)
TOTAL CASES	77	23	100

* Includes indeterminate or unsatisfactory examinations.

TABLE 1B: COMPARISON OF INITIAL ROENTGENOLOGIC AND GASTROSCOPIC EXAMINATIONS IN 100 GASTRIC ULCERS

	Roentgenologic Examination	Gastroscopic Examination
Per cent of all lesions detected	91%	86%
Per cent detected lesions correctly interpreted	91.2%	91.2%
Overall accuracy of detection and interpretation	83%	81%
Overall accuracy of combined methods of examination*	95%	

* Although only 3 lesions were incorrectly interpreted by both methods (97 per cent overall accuracy), 2 additional cases correctly interpreted radiologically as benign ulcers were subjected to surgery since the gastroscopist felt that tumor could not be excluded. These, therefore, are considered as errors. In all other instances of disagreement, the information obtained by one method of examination was felt to be sufficiently documented to take precedence over the findings of the other.

cers were subjected to surgery since the gastroscopist felt that tumor could not be excluded. These, therefore, are considered as errors. In all other instances of disagreement, the information obtained by one method of examination was felt to be sufficiently documented to take precedence over the findings of the other. An analysis of the failures of each method affords a striking example of the fashion in which the two procedures supplement each other.

Of the 9 roentgenologic failures in benign disease, 8 were superficial gastric ulcerations which were not detected. Four of these were definitely in the healing stage and measured 4 mm. or less in diameter. Of the remaining 4, 1 lay on the greater curvature (Fig. 8; B in color plate), 1 on the posterior wall of the gastric antrum, 1 high on the anterior wall of the body, and 1 on the gastric side of a gastrojejunostomy

Fig. 10. Filled pseudo-radiation between incisura area. See D in

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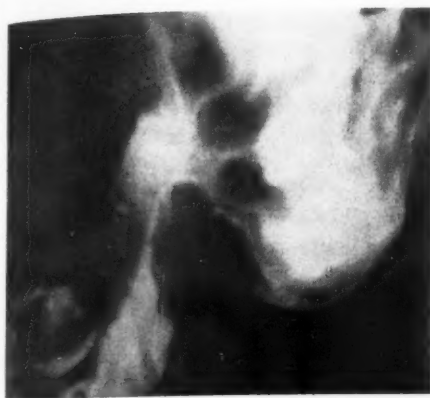


Fig. 10. Malignant ulcer in region of incisura angularis. Film from upper gastrointestinal series showing pseudo-radiating mucosal folds as a result of barium between marginal tumor nodules. The opposing "incisura" is frequently seen in tumors involving this area. Both may be misinterpreted as signs of benignity. See D in color plate.



Fig. 11. Malignant ulcer misinterpreted roentgenologically. Cuff of tumor at ulcer orifice interpreted as collar. In retrospect the cuff is irregular and definite tumor nodules are visible on greater curve aspect (arrow). Lack of distensibility and "incisura" attributed to spasm. Ulcer diameter had decreased one-third in size in three weeks on comparison with study done elsewhere. See E in color plate.

stoma. The remaining benign lesion was a large (1 cm. in greatest diameter) but superficial greater-curvature ulcer which was detected and classed as indeterminate because of the marked induration of the adjacent stomach wall.

Four of the 5 malignant ulcers classified as radiologic failures were detected. Two were interpreted as benign and 2 as indeterminate. The fifth was associated with a benign ulcer, which was noted. In retrospect, 4 of these cases demonstrated radiographic features which either suggested or clearly indicated malignant disease. All of the lesions were identified and correctly interpreted gastroscopically (Fig. 11; E in color plate).

Of the 16 gastroscopic errors, 10 involved prepyloric lesions which could not be visualized. One of these was malignant (Fig. 12). One small benign ulcer in a hiatal hernia was not seen, and 2 large benign ulcers were designated as malignant (Fig. 9; C in color plate). Three examinations were unsatisfactory. In each instance a correct radiographic diagnosis was reached.

Both examinations were incorrectly interpreted in 3 instances. It is significant that the failures of detection with one modality occurred in areas more suited to



Fig. 12. Ulcerating carcinoma of gastric antrum. This lesion could not be visualized gastroscopically. The lesser curvature aspect of the antrum remains a gastroscopic "blind spot."

the other procedure. If disease of the prepyloric area is excluded, only 4 lesions, including 3 unsatisfactory examinations, would have been undetected gastroscopically. Similarly, with the exclusion of

superficial and minute healing ulcers, but 1 lesion would have been undetected roentgenologically.

The ability of both methods to interpret correctly a visualized lesion was approximately the same, and the major interpretive errors with the combined approach were associated with perforated or penetrating lesions.

Although gastric cytologic studies were not employed in a sufficient number of patients to warrant their inclusion in this report, it seems probable that utilization of all three methods would increase the accuracy of clinical evaluation beyond 95 per cent. In 2 cases of benign ulceration seen since the compilation of this material, diffuse associated gastric fibrosis led to roentgenologic and gastroscopic diagnoses of extensive cancer. In each instance the cytologic studies were negative. Preliminary evaluation indicates a high degree of correlation between the three procedures.

DISCUSSION

The case for the surgical treatment of all gastric ulcers has been well stated by Comfort *et al.* (6) in their statistical analysis of 1,005 small (4 cm. or less in diameter) benign and malignant gastric lesions. Of these, 226 were cancers, all but 3 of which were ulcerating. In the malignant group the correct diagnosis was made or suggested roentgenologically in 69.3 per cent. In the remaining 30.7 per cent the roentgenologist did not detect the features suggestive of cancer. The mortality rate for subtotal gastrectomy in the group of small cancers was 1.8 per cent as opposed to 6.4 per cent for partial gastrectomy performed in 830 cases of gastric cancer of all sizes during the same period. In addition, the five-year survival rate for small cancers was 40 per cent greater than that for gastric cancer of any size. Surgical treatment of 779 benign ulcers seen during the same period was accomplished with an overall mortality rate of 1.5 per cent and a ten-year survival rate equal to that of a normal population of the same age and sex. In patients with benign disease,

the operative result was considered satisfactory in 86.7 per cent. Comfort and his associates acknowledge the value of the roentgenologic examination, citing an 87 per cent overall accuracy in those lesions specifically designated as benign or malignant. They conclude, however, that operative proof of malignancy in 60 per cent of 55 patients adjudged roentgenologically to have benign disease is a justification for surgical therapy.

Such results do not necessarily imply that the radiologist or gastroscopist must become an advocate of indiscriminate surgical therapy once an ulcer has been demonstrated. Although 22.2 per cent of the ulcerative lesions in Comfort's series were malignant and the average incidence of cancer in 3,349 gastric ulcers compiled from the literature (5, 7, 12, 17, 18) is 13.8 per cent, it is impossible to determine how many of these actually mimicked benign ulcers. Stout (30) found a 6 per cent incidence of malignant penetrating ulcers among 470 stomachs resected for carcinoma. He states that each of these had all of the gross attributes of a benign ulcer, but that carcinoma was found along one margin or completely surrounding the edge without involvement of the base. It is our belief that this is the more realistic figure when clinical criteria are carefully applied to the individual ulcer. From the roentgenologic standpoint, 91.2 per cent of the visualized lesions in this series were correctly interpreted, and retrospective study indicates that misinterpretation of 4 out of 5 ulcerating cancers was the result of individual error rather than failure of the method. Similarly, 94.2 per cent of detected lesions were correctly interpreted gastroscopically. These results, and the overall accuracy of 95 per cent with the combined procedures, correlate well with the 6 per cent figure of Stout.

Unfortunately, many of the results of surgical therapy reported in the literature do not parallel those of Comfort. The incidence of mortality and morbidity fluctuate both with the surgeon and the type of procedure employed. Present mortality

rates for subtotal gastric resection average between 2 and 3 per cent, and, in general, it may be stated that the higher the resection, the higher the mortality rate. In a collected series of 1,726 patients who had total gastrectomies between the years 1950 and 1954 (17), the average mortality rate was 25.3 per cent. At present, even in the best of hands, an average mortality rate of 9 to 12 per cent is to be expected.

The frequency of postoperative morbidity is more difficult to determine. According to Jordan (13) the incidence of the dumping syndrome as reported in the literature varies from 2 to 45 per cent of patients who have undergone some type of subtotal gastrectomy. There are many possible explanations for these discrepancies, but it is his belief that only about 15 per cent have symptoms of sufficient severity to require treatment. Other post-gastrectomy difficulties include impaired nitrogen assimilation, decreased fat absorption, nausea, vomiting, diarrhea, and marginal ulcer. Regardless of the variability of the statistics, it seems evident that there will be a group of patients who will spend their postsurgical lives with some degree of discomfort attributable to surgery. The statement that the patient has been willing to trade the discomfort of his ulcer for that of the milder post-operative complaints is not necessarily a valid criterion for the acceptance of surgical therapy since many have not been given an opportunity to evaluate their sense of well-being following an adequate trial of medical treatment. While it is often estimated that between 30 and 40 per cent of all patients with benign gastric ulcers will eventually require operation for some form of complication, this still leaves a potentially large number for whom a relatively normal life is possible, a particularly important consideration in the younger age groups.

Evidence of the efficacy of medical criteria in differentiating benign from malignant gastric ulcers is offered by Dworken *et al.* (8). These authors made a final diagnosis of benign gastric ulcers in

135 patients on the basis of the following criteria: (a) benign appearance of the ulcer on x-ray or gastroscopic study; (b) the presence of free acid on gastric analysis, (c) complete relief from symptoms on treatment; (d) complete radiologic healing of the ulcer crater. Of the 135 patients, 130 were followed for an average of forty-six months. Two were found to have carcinoma of the stomach. In each, failure to obtain radiologic evidence of lack of ulcer healing before discharge was considered the probable cause of misdiagnosis. Two others thought to have benign ulcers at the beginning of therapy were eventually operated upon because of nonhealing and were found to have malignant lesions.

While complete healing of a gastric ulcer with restoration of the mucous membrane pattern and flexibility of the regional wall is the most convincing evidence of benignity, discussion of that feature as a differential diagnostic criterion has been delayed until this point since it is useful only after initial evaluation of the ulcer has indicated a suitable candidate for medical therapy. The application of the radiologic and gastroscopic criteria for selecting such patients can be summarized by the statement that the most important single finding is the presence or absence of mass. The function of such roentgenologic findings as Hampton's line and the ulcer collar may be considered as supportive rather than definitive; as in Figs. 4, C and D, the presence of Hampton's line may throw the weight of opinion toward a benign ulcer despite the resemblance of the "ulcer mound" to a meniscus sign. Conversely, Hampton's line or an ulcer collar in the presence of unequivocal mass should not be considered significant diagnostic points. Gastroscopecally the same general statement may apply. Mucosal inflammatory changes or other findings usually associated with benign disease are not pertinent when definite infiltration of the ulcer margin or adjacent mucosa can be demonstrated.

Once it is concluded that a trial of

medical management is warranted, it is essential that it be carried out in a hospital as a carefully controlled program. While it is commonly stated that a benign ulcer should heal or nearly heal in three weeks, this rule of thumb is open to considerable question, and six weeks is probably a more realistic arbitrary limit. Healing should be complete and, with the exception of the occasional fibrosing antral lesion, leave little or no residual deformity. Persistent distortion of the gastric wall near or at the site of a healed or healing ulcer should always suggest the possibility of cancer. It is often stated that malignant ulcerations can and will heal. Schindler (25) has described a case in which a crater was obliterated by tumor tissue. Kirsh (15) reports an example of partial healing in two weeks and 2 others with complete healing in six weeks followed in 1 by the appearance of tumor mass. Strandjord (31) and his colleagues encountered 2 cases, and 1 malignant crater in our series decreased approximately one-third in size in three weeks (Fig. 11; E in color plate). Such instances, however, are the exception rather than the rule. The acceptance of healing as an indication of benign disease has proved quite reliable in our institution *provided the radiologic findings are confirmed gastroscopically*. As noted by Templeton (32), an ulcer which is filled with neoplastic tissue may be indistinguishable radiologically from true healing. The difference is readily apparent gastroscopically when the site of ulceration is within range of the instrument. In the gastroscopic service at M. D. Anderson Hospital, no carcinomatous ulcer has been seen to heal, a fact which makes endoscopic follow-up desirable in the questionable lesion. Without gastroscopic control, decrease in the size of an ulcer is not a totally satisfactory indication of benignity, since only a portion of the ulcer may contain malignant tissue and the benign segment is, at least theoretically, capable of responding to conventional therapy. Conversely, lack of healing alone cannot be considered pathognomonic of neoplastic disease, since

benign penetrating ulcers and benign ulcers in the arteriosclerotic patient are notoriously resistant to treatment.

If response to therapy is inadequate or if an ulcer recurs, the stomach should be resected unless there are other factors which contraindicate surgery. Aside from the morbidity of gastric ulceration, the necessity for intervention in the refractory or recurrent ulcer is underlined by Smith and his co-workers (29) who, in a series of 1,000 gastric ulcers, found that carcinoma occurred in 18.5 per cent of those classified as intractable and in 18.5 per cent of those designated as recurrent.

The fact that a small percentage of apparently benign ulcers will fail to respond to medical therapy and prove malignant upon resection does not mitigate against therapeutic trial. The majority of cancers evolve slowly, and it is not probable that a three to six weeks delay in the doubtful case will seriously compromise the chances of survival should the lesion prove malignant.

COMMENT

If the foregoing results and conclusions are accepted as valid reasons for advocating clinical evaluation of gastric ulcers, then comment upon failure of their complete acceptance is warranted. Just as the abilities and training of the individual surgeon vary, so do those of the physician performing the roentgenologic or gastroscopic examination. As pointed out by Palmer (19), not everyone with a gastroscope is a gastroscopist. Nor is everyone who performs gastrointestinal roentgen studies a roentgenologist. The margin for error with either method of evaluation has been further enhanced by the number of differential criteria suggested. Since the roentgenologic description of the ulcer niche by Houdek in 1913 and the perfection of the flexible gastroscope by Wolfe and Schindler in 1932, a massive amount of material has been contributed. Unfortunately, many of the criteria have been based upon an inadequate number of cases and have not

withstood the test of time; yet it is not at all uncommon to find these statements perpetuated in the current literature.

An additional deterrent to the clinical evaluation of gastric ulceration has been an attitude of competition which has existed between the gastroscopist, the radiologist, and, more recently, the cytologist. Such competition is useful when it stimulates individuals in each field to greater effort to improve the efficacy of a particular instrument; it is unwise when over-enthusiasm prevents appreciation of the worth of others. It should be obvious that in a problem of such serious import to the patient, parochial enthusiasm should be discarded.

Although gastroscopy ideally complements the roentgenologic study in the discovery, differentiation, and serial evaluation of gastric ulceration, considerable experience, which can be obtained only by routine employment, is necessary for proper use of the instrument. The gastroscopist should be utilized not only when assistance is required in the classification of a roentgenologically visualized lesion, but also in those patients with gastrointestinal symptoms who have negative x-ray examinations. Such routine use not only increases the skill of the endoscopist but may reveal superficial or frank ulceration in areas of poor roentgenologic visibility.

The use of newer instruments, especially those with controllable tips, has helped to eliminate gastroscopic "blind spots," such as portions of the fundus and lesser curvature of the body of the stomach, which were formerly poorly seen. The lesser curvature of the antrum and the pylorus remain difficult to visualize. Inflammatory changes in the gastric mucosa or submucosal tumor infiltration may prevent visualization of an ulcer, although indicative of its probable origin. Severe inflammatory infiltration of the ulcer margin may be interpreted as neoplastic. Such failures, as well as the inexperience of an occasional endoscopist, have at times cast doubt upon the usefulness of the method. Where it is used in close co-

operation with roentgenology, however, a clear picture of ulcer pathology will emerge in the great majority of patients.

Gastroscopic color photography, now available and reliable, helps to document the ulcer characteristics for the gastroscopist and radiologist. Features demonstrated by both methods can be compared and evaluated and endoscopic training facilitated. Such photographs are quite comparable, in their way, to roentgenograms and may be filed for serial study in the same manner.

SUMMARY AND CONCLUSIONS

1. The results of combined radiologic and gastroscopic evaluation in 100 cases of gastric ulceration are presented.

2. Radiographic and gastroscopic criteria are enumerated which have, in our experience, proved reliable in the differentiation of the benign from the malignant ulcer.

3. The routine documentation of gastroscopic findings by intragastric color photography considerably enhances the value of the procedure and does much to dispel the skepticism which was formerly accorded the written gastroscopic report.

4. It is concluded that gastroscopic examination ideally complements the roentgen study in the discovery, differentiation, and serial evaluation of gastric ulceration. The major interpretive errors with the combined approach occurred with perforated or penetrating gastric ulcers. Ideally the latter should, in most instances, be considered as indeterminate—a group which should average about 5 or 6 per cent within the areas of competency of both procedures.

5. The overall accuracy of the combined approach is sufficiently high to warrant a trial of therapy in the patient in whom no suggestion of malignant disease is seen. It is concluded that a blanket policy of gastric resection for all cases of gastric ulceration is undesirable and unnecessary.

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SUMMARIO IN INTERLINGUA

Le Combinate Evaluation Radiologic e Gastroscopic de Ulceration Gastric

Es presentate le resultatos del combinate evaluation radiologic e gastroscopic in 100 casos de ulceration gastric. Es enumerate le criterios radiographic e gas-

troscopic que se ha provate, in le experientia del autor, como digne de confidentia in le differentiation inter ulcers benigne e maligne. Le documentation routinari

del constataciones gastroscopic per chromophotographia intragastric augmenta considerabilemente le valor del methodo e servi excellentemente a dispeller le scepticismo le qual—in le passato—characterisava le reception accordate al manuscripte reporto gastroscopic.

Es concludite que le examine gastroscopic complementa idealmente le studio roentgenologic in le discoperta, differentiation, e evaluation serial de ulceration gastric. Le major errores de interpretation occurrente in le uso del combineate methodology concerneva grande perforate

o penetrante ulcers gastric. Iste ultimes—in le majoritate del casos—es idealmente a considerar como indeterminate. Illos constitue un gruppo que include, al media, 5 o 6 pro cento del casos intra le area de competentia del duo methodos.

Le accuratia general del combineate methodology es sufficientemente alte pro justificar un essayo de therapia medical in le patiente in qui nulle indication de malignitate del morbo es notate. Un strategia universal de resection gastric in omne casos de ulceration gastric es indesirabile e innecessari.



Radiologic Diagnosis of Polyps of the Colon in Children¹

D. W. MacEWAN, M.D., and J. S. DUNBAR, M.D.

BECAUSE OF THE importance of early and accurate recognition of polypoid lesions of the colon, in order to prevent death from cancer, the emphasis in radiologic diagnosis of colonic polyps has been upon the adult patient (2, 4, 8, 10, 11). The polyps found in childhood are not precancerous (6), except in familial multiple polyposis, and bleeding per rectum is the chief clinical problem. The rigors of preparation and the co-operation needed from the patient in the performance of a barium-enema study make the direct application of adult procedures awkward in children. This report presents the experience in The Montreal Children's Hospital from 1946 to 1959 with polyps of the large intestine and describes a simple and accurate method of radiologic diagnosis.

RADIOLOGIC EXAMINATION

The method of radiologic search for polyps of the colon is basically that described by Christie, Coe, Hampton, and Wyatt (4), modified to permit examination of the entire mucosa. It was found that several enemas over a short time with a 1 per cent tannic acid barium mixture caused complete evacuation of the colon and produced a good mucosal pattern.

The initial decision to search for polyps is usually easily made (5, 7). The child is likely to be two to seven years of age, with a history of painless passage of bright red blood with stool on one or more occasions, and other clinical features as listed in Table 1, Section F. No castor oil or other oral laxatives are used, as they are difficult to administer, and saline enemas the evening before and the morning of the examination have been found adequate. Examination may indeed be begun with no preparation at all. One and one-half quarts of a warm 1 per cent tannic acid mixture of barium and water is prepared.

This is thoroughly stirred and the stagnant fluid in the tubing is run off just before each filling of the colon. Thorough mixing is essential for adequate coating of the bowel wall.

The first filling is made to the distal portion of the transverse colon and the child is allowed to evacuate immediately. Children are found to evacuate better sitting on the toilet, and the bedpan is used only if they cannot sit. Several more fillings and evacuations are usually necessary before visualization of the entire colon is obtained. The first enema is the most distressing; the subsequent ones are easier to administer and evacuation is more prompt. The number of enemas rarely exceeds three or four, but a single filling is almost never adequate.

Fluoroscopy is sparingly used; the field is small and the time usually does not exceed two minutes. Further reduction in irradiation of the child is now being achieved by the use of image intensification. No detailed fluoroscopic search for lesions is made; the chief concern is to avoid excessive filling of the colon, with subsequent reflux into the ileum, which would obscure the sigmoid colon. The later fillings may be made as far as the hepatic flexure but not beyond that point, since otherwise spill into the ileum is likely to occur. When the contents of the colon have been completely evacuated, fluoroscopically controlled films are made in the anterior, lateral, and both oblique projections; all portions of the colon should be unfolded and well visualized by these radiographs. The lateral view has been particularly useful in the examination of the sigmoid colon and rectum, and often a slightly off-lateral projection is made as well.

Figure 1, A illustrates the colon after the fourth filling and evacuation of the

¹ From the Department of Radiology, The Montreal Children's Hospital, Montreal, Canada. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

TABLE I: POLYPS AT THE MONTREAL CHILDREN'S HOSPITAL 1946-1959 INCLUSIVE

A. Case Material 151 cases (6 patients returned later with supposedly new polyps): 87 males; 64 females.													
B. Age Distribution													
Age in years	0	1	2	3	4	5	6	7	8	9	10	11	12
Number of cases	0	1	7	34	36	28	17	10	3	7	3	6	5
C. Number of Polyps Proved per Case													
Number of polyps	1	2		3	4	5	6	7	8	9	10	11	12
Number of cases	99	28		14	5	5	...	2	2	1	1
D. Polyp Sites													
Rectosigmoid	199	High Sigmoid		Descending		Transverse		Ascending		Cecum			
		32		35		23		3		1			
E. Yearly Analysis of Cases													
Year	Cases	Barium Enema		Polyps Found		Polyps Missed		Polyps Over-Diagnosed					
1946	2	2		0		2		2					2
1947	1	1		2		2 (2 sigmoid)		0					0
1948	1	1		0		2		0					0
1949	4	3		1		2 (1 sigmoid)		0					0
1950	6	1		0		1		0					0
1951	15	10		9		15 (1 trans.; 8 sigmoid)		0					0
1952	12	11		13		3		6					6
1953	11	11		12		12 (1 trans.; 1 sigmoid)		1					1
1954	22	17		15		12 (1 sigmoid)		0					0
1955	17	14		16		6		0					0
1956	11	9		13		14 (2 descending)		0					0
1957	20	20		24		5		0					0
1958	14	13		22		5		0					0
1959	20	18		22		2		1					1
TOTAL	157	132*		149		83 (17 not rectal; 7 above sigmoidoscopy)		10					
* 61 polyps removed from patients who did not have barium-enema examination.													
F. Symptoms and Signs													
Blood in bowel movements						145							
Protruding polyps seen						31							
Pain						29							
Palpable mass in rectum						28							
Prolapse of rectal mucosa						8							
Polyp passed and identified pathologically						3							
Constipation						2							
Excessive blood loss						4							
G. Review of Surgical Experience													
All rectosigmoid polyps removed at endoscopy													
1 bowel obstruction after removal of sigmoid-polyp by cautery.													
33 laparotomies performed for high polyps													
5 bowel obstructions													
2 wound dehiscence													
No deaths													
H. Miscellaneous Observations													
Polyps passed spontaneously months later under observation						3							
Polyps followed without operation						8							
Mucosal intussusception shown radiologically						7							
Siblings with colonic polyps						4							
Unsuspected polyps found in 420 postmortem examinations						4							

mixture and Figure 1, B demonstrates the mucosal pattern after the fifth filling and evacuation. Figures 1, C, D, and E are oblique and lateral projections visualizing the entire rectum and sigmoid colon. Although contrast material was never run beyond the hepatic flexure, the cecum and ascending colon are well visualized due to reflux, which occurred in almost all of our examinations. These films show a fine feathery mucosal pattern which is

normal in appearance. At sigmoidoscopy no polyps were found, and no further bleeding has occurred, confirming the radiological diagnosis of a normal colon.

Occasionally delays may be caused when reflux of the barium mixture into the ileum obscures the sigmoid colon. The child is then fed and the examination is resumed a few hours later. By this time the barium in the terminal ileum has passed into the colon. Examinations are thus completed

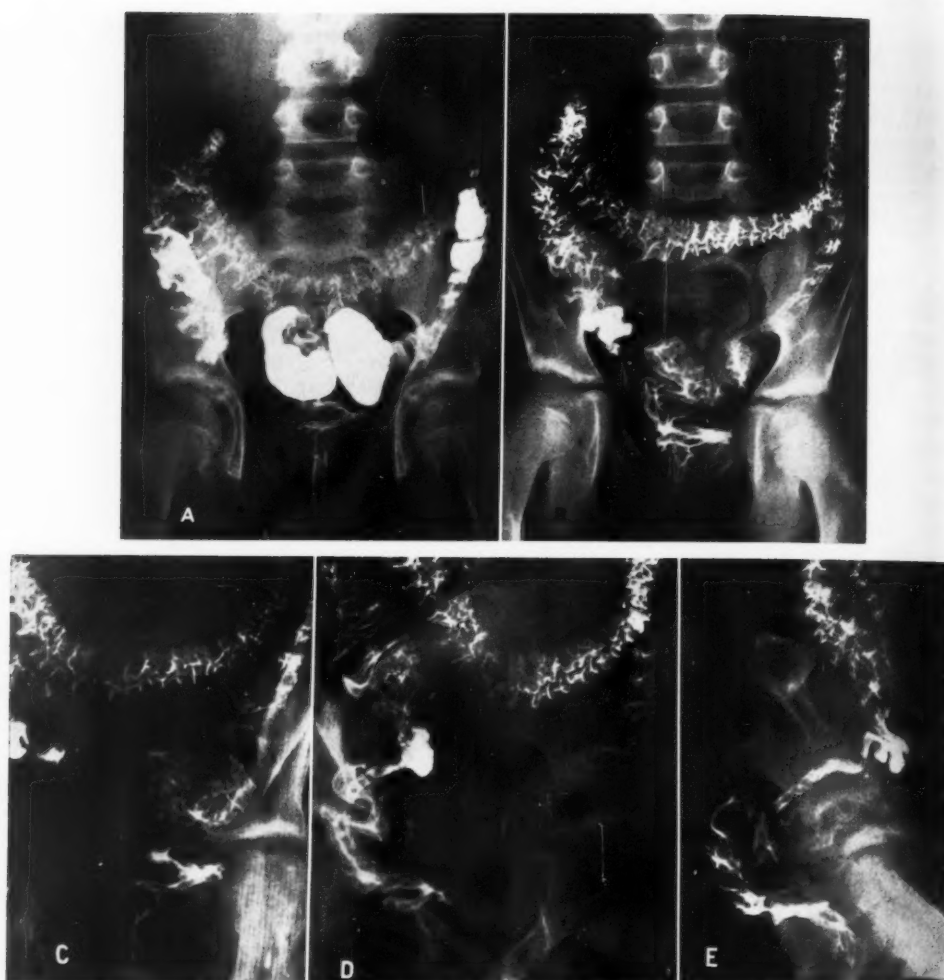


Fig. 1. Method of search for polyps of the colon in children.

- A. Four fillings and evacuations. Colon not fully evacuated.
- B. After fifth enema and evacuation the colon is well emptied, showing a normal mucosa. The rectosigmoid region is unfolded in the oblique and lateral views (C-E).
- C. Right anterior oblique projection.
- D. Left anterior oblique projection.
- E. Lateral projection.

on the day the patient is referred for radiologic study.

The radiographs must be obtained promptly after evacuation, as the mucosal pattern begins to deteriorate in a few minutes. This has not been previously stressed but is important for two reasons. First, this method of examination is dependent upon an exquisite record of the entire mucosa. Figure 2 shows the good

mucosal demonstration made less than five minutes after evacuation (A); ten minutes later (B) the distal half of the colon can no longer be assessed. In the second place, if the mucosa does not appear normal after repeated enemas, inflammation of the colon may be suspected. In 3 such cases in our experience, colitis was subsequently proved. One child (Fig. 3), originally referred with a provisional diagnosis of

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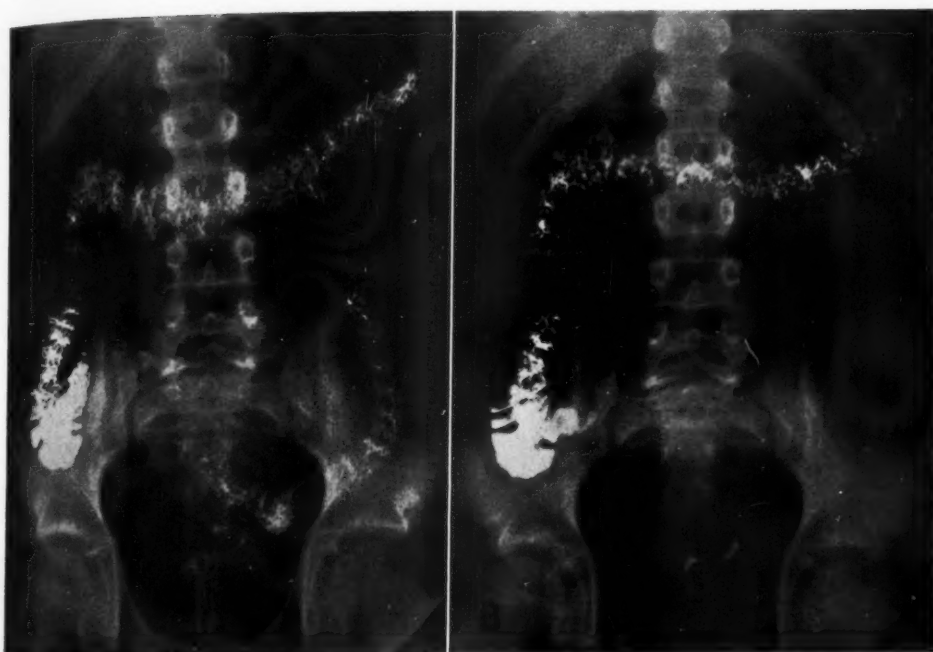


Fig. 2. Deterioration of mucosal pattern with time.

- A. Radiograph made less than five minutes after evacuation, showing good mucosal pattern of entire colon.
 B. Radiograph of same patient made ten minutes later. The distal half of the colon can no longer be assessed.

colonic polyps because of rectal bleeding, proved to have ulcerative colitis. Another also had ulcerative colitis, while the third had a *Shigella* infection.

One contraindication to this method of investigation is recent proctoscopic or sigmoidoscopic examination. The passage of rectal tubes in children who have just undergone these procedures is extremely painful, and the moderately irritating mixture adds to their discomfort. They cannot be expected to co-operate under these circumstances. The radiologic examination should therefore precede endoscopy.

For the past few months a suspension of 15 mg. of bisacodyl (Dulcolax²) in water has been added to the barium, water, and

²Boehringer Ingelheim Products, distributed by Geigy Pharmaceuticals (Canada) Ltd.



Fig. 3. Recognition of colitis. Roentgenogram made after third evacuation showing very poor mucosal detail in rectum and sigmoid colon. Typical lesions of ulcerative colitis found several days later at sigmoidoscopy.



Fig. 4. Comparison of single and double contrast techniques.

- A. Sigmoid polyp demonstrated.
 B. Air-contrast enema of same patient showing the polyp. Overlap of distended bowel wall often makes it difficult to visualize all parts of the distal colon.

tannic acid mixture. Better evacuation has thus been achieved, and one or two less fillings of the colon have been necessary for good studies. The procedure has now been incorporated into our technic, and so far has not led to any lessening of diagnostic accuracy, while the reduced number of fillings has simplified the examination for both patient and radiologist. The efficacy of the mixture is borne out by two observations: (a) its use in routine barium enemas for purposes other than a search for polyps has resulted in excellent mucosal studies of nearly the entire colon; (b) a single saline enema containing bisacodyl one hour before the examination has been successfully used in preparing patients for all forms of radiography.

CLINICAL MATERIAL

Table I summarizes our experience with 151 children with polyps of the colon studied from 1946 to 1959, inclusive, at The Montreal Children's Hospital. Six returned later with supposedly new polyps, so that 157 studies were made. Section A

records the sex incidence; the cases are grouped in Section B according to age at the time of investigation, and in Section C according to number of proved polyps. Section D gives the sites of the polyps, "rectosigmoid" referring to those found by proctoscopy or sigmoidoscopy and "high sigmoid" to those beyond the reach of these procedures.

In Section E, the cases are analyzed on a year-by-year basis. "Barium enema" signifies pretreatment barium examinations; "polyps found" shows the number of polyps correctly diagnosed by barium enema; "polyps missed" refers to rectal polyps unless otherwise specified; and the last column, "polyps over-diagnosed," records those instances in which the radiologic diagnosis of polyp was not proved by direct visualization, surgical exposure, or serial enemas.

The incidence of different symptoms and signs is shown in Section F. Pain as a presenting symptom is difficult to assess as most of the children with this complaint were in the older age group and half of

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them described only vague abdominal pain with poor relation to bowel movements. Diarrhea was not recorded in the charts reviewed, although it has been found in other series (7). Four of the children had excessive blood loss, requiring transfusion, and for this reason colon polyps must be considered in the differential diagnosis of massive melena. The review of surgical experience, Section G, is included since bowel obstruction was a common complication, and this is of radiologic importance. Section H contains miscellaneous observations.

RADIOLOGIC DIAGNOSIS

The diagnostic accuracy of radiologic search for colonic polyps has not until recently been considered satisfactory at The Montreal Children's Hospital. The examinations from 1946 to 1954 were mostly single contrast studies with variable degrees of evacuation and mucosal definition. Some double-contrast enemas were performed, but the procedure was unsatisfactory, due for the most part to technical difficulties, such as poor co-operation of the child, overlap of loops of distended

bowel (see Fig. 4), residual barium obscuring portions of the colon, and elongation of the distended bowel, making it impossible to show the entire colon on a single radiograph in the smaller children.

Beginning in 1952, more emphasis was placed on obtaining a good mucosal pattern. Initially, the portions of the

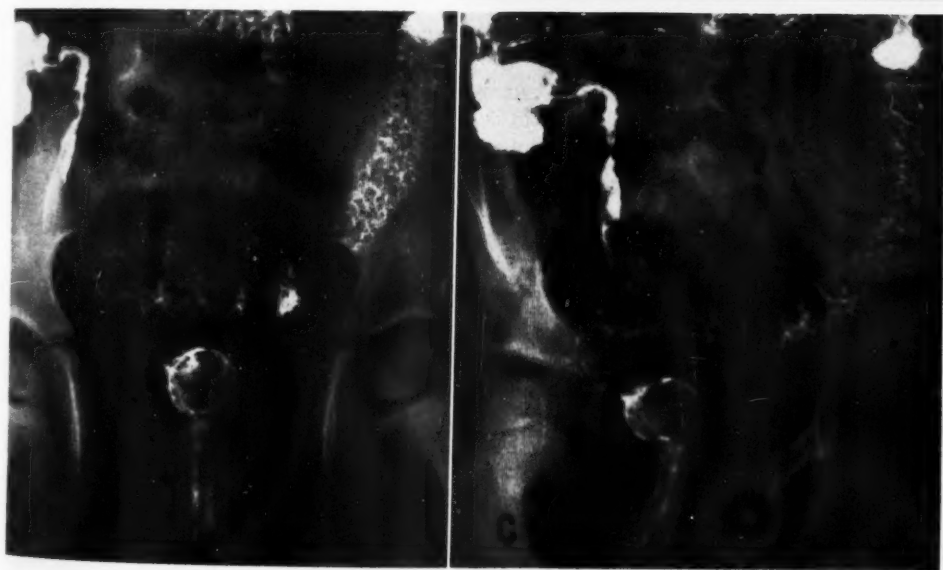
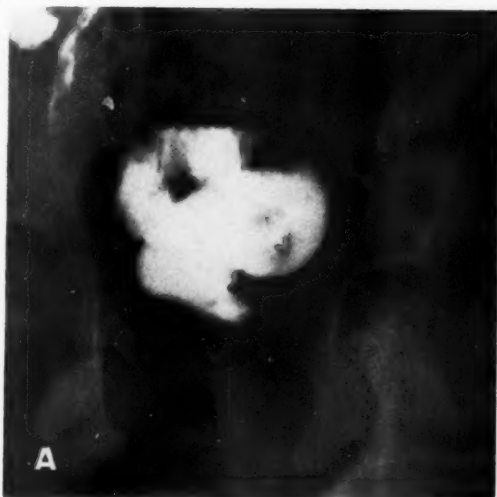


Fig. 5. Recognition of polyp.

- A. Incomplete evacuation of sigmoid colon; polyp seen displacing barium.
- B. Anteroposterior view. Sigmoid polyp well seen after complete evacuation induced by one more enema.
- C. Right anterior oblique projection showing the polyp.

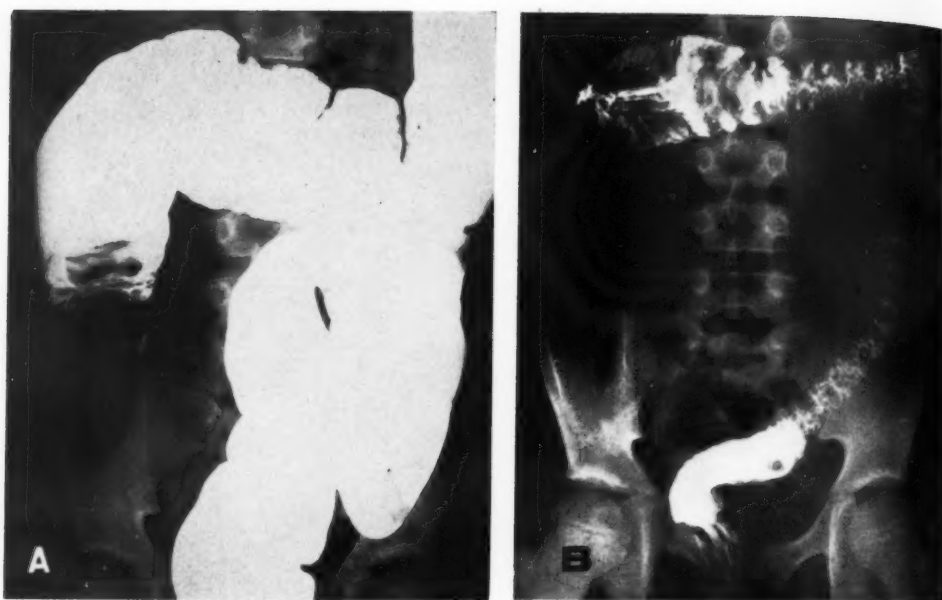


Fig. 6. Mural intussusception.

- A. Large mass in ascending colon outlined by barium column.
 B. On evacuation the mass moves to the transverse colon and leads a colocolic intussusception.

colon above the reach of the sigmoidoscope were the chief concern. Success with observation of this portion of the bowel and the discovery that lower polyps could also be diagnosed accurately following total evacuation has since 1957 led to a reduction in the number of errors. For example, in 1959, when our studies were most thorough, 22 polyps were found, and only 2 small rectal polyps were missed. These might also have been discovered with more complete evacuation of the colon. One "over-diagnosis" is listed in 1959. In this instance the lesion was in the mid portion of the sigmoid colon; it could not be visualized at sigmoidoscopy and laparotomy was not performed. For record purposes, therefore, this is considered as an over-diagnosis, although the roentgenograms strongly suggested a polyp. The value of barium-enema investigation of the colon is illustrated by 2 recent patients in whom sigmoid polyps were found by this means, were not seen on initial sigmoidoscopy, were again demonstrated on barium studies, and were finally identified on a

second sigmoidoscopic examination and removed.

The Polyp: The chief criterion for radiological diagnosis of a polyp is a rounded space-occupying lesion which interrupts the normal feathery pattern of the freshly coated, contracted bowel. Figure 5 illustrates a polyp occupying space in an incompletely evacuated colon (A). Following a further filling of the colon, complete evacuation was achieved and the polyp is well shown (B and C). When there is concern that a round shadow may represent fecal matter, the colon is again filled and evacuated; if the shadow does not change in position, it is almost certainly a polyp. This is important, as with double-contrast enema studies suspected lesions must usually be reinvestigated by examinations on a later occasion. Size of the lesion is not of too great diagnostic importance. Polyps as small as 0.4 cm. in diameter were diagnosed correctly, while others over 2.5 cm. were missed (by what we now consider poor technique). Fecal matter fixed to the bowel wall has not been

encountered in our series of children (9).

The Pedicle: The finding of a pedicle is helpful in identifying accurately the nature of the lesion (11). The pedicle (Figs. 7 and 8) appears longer on roentgenograms than at sigmoidoscopy or at laparotomy, as the colon is not in a state of active contraction during surgical visualization.

Intussusception: Two forms of intussusception are defined by us, mural and mucosal. *Mural intussusception*, in which

Mucosal intussusception, in which the intussusceptum apparently consists only of mucosa, is clinically silent and benign. This phenomenon was encountered in 7 patients, 2 of whom were followed for several years, with the intussusception appearing on all but one occasion. Figure 7 illustrates a mucosal intussusception led by a polyp; there is a second polyp in the descending colon, and a third in the transverse colon near the hepatic flexure. Al-

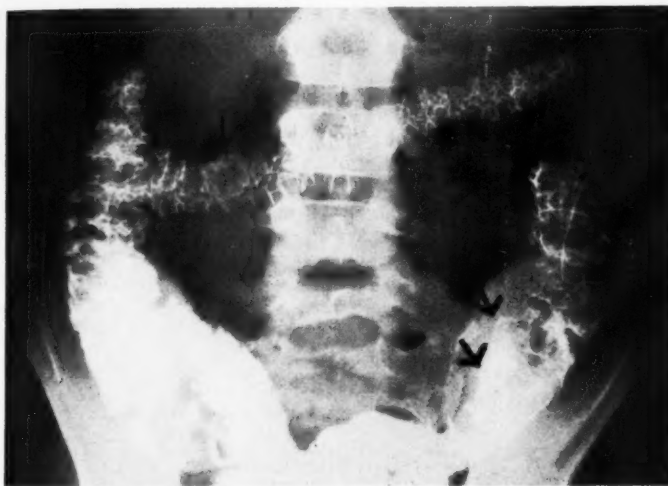


Fig. 7. Mucosal intussusception. The polyp indicated by the middle arrow leads a mucosal intussusception. The pedicle is partly shown pointing to the polyp. Two other polyps are present.

the intussusceptum includes the full thickness of the bowel wall, is the familiar type, with a well known clinical picture in childhood. In a review of 150 bowel intussusceptions at this hospital (3), 2 were found to be initiated by a polyp of the colon. One patient, an eight-year-old girl, had a bleeding mass protruding through the anus, which reduced spontaneously. A barium-enema study showed a rounded lesion (Fig. 6, A) at the head of the barium column in the ascending colon. On evacuation, a colocolic intussusception (Fig. 6, B) was shown, led by a large polyp. At laparotomy a 3-cm. polyp of the ascending colon was removed. The second child had three polyps removed from the descending colon following operative reduction of an intussusception into the sigmoid colon.

though this phenomenon has not been emphasized by previous authors, an illustration in the article by Christie *et al.* (4) shows it well. At operation no damage to the bowel wall has been encountered in these patients, and none have had mural (classical) intussusception or other complication. The radiologic appearance in these circumstances is decisive, including mucosal intussusception, pedicle, and polyp.

INCIDENCE OF COLONIC POLYPS

The true incidence of childhood polyps of the colon is not known, nor is the mechanism of their disappearance fully understood. The age distribution in our series, as shown in Table I, is similar to that in other reported series (5, 7). Most polyps

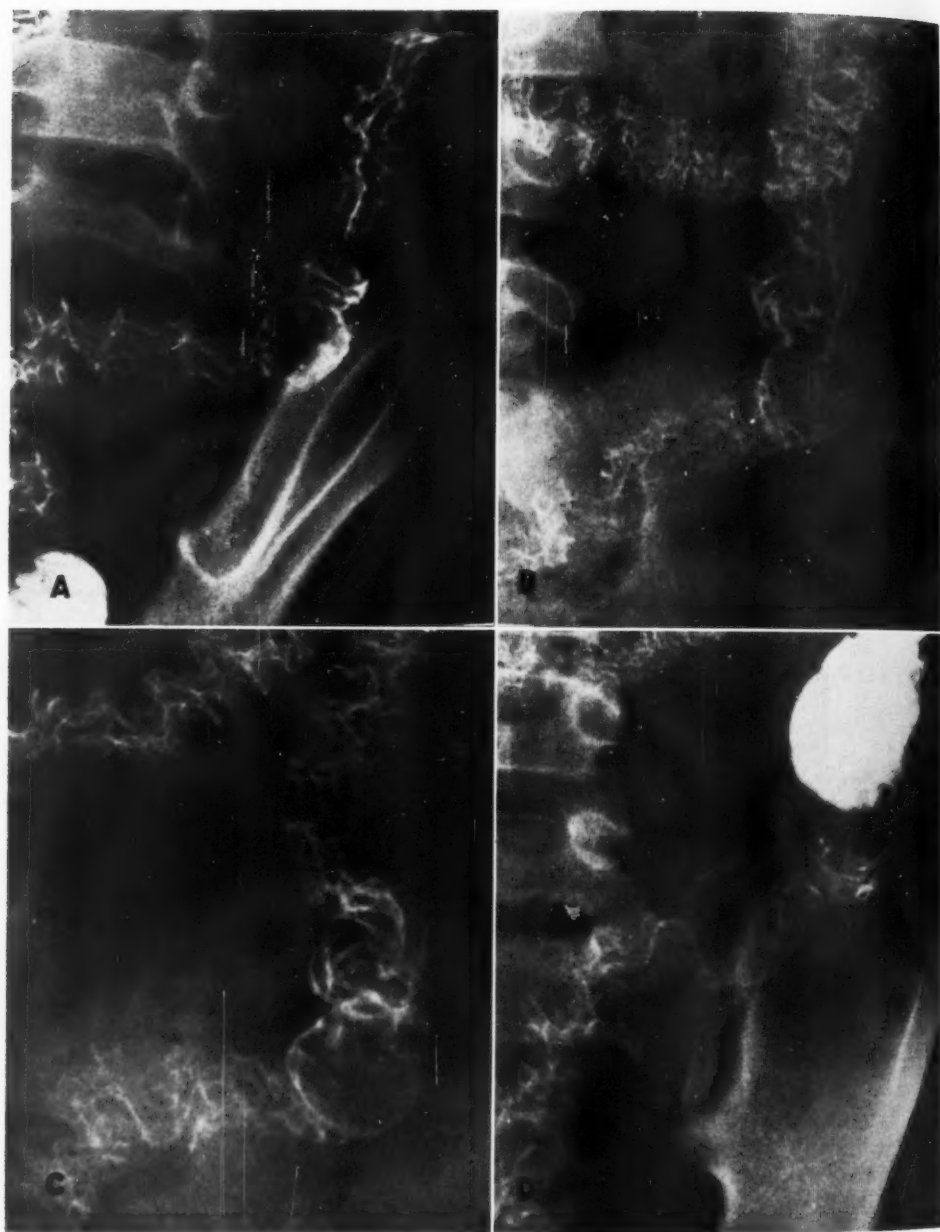


Fig. 8. Polyp of descending colon with mucosal intussusception; serial barium enemas.
 A. Initial discovery after moderate rectal bleeding. Operation not done as the child had previous colotomy for polyps.
 B. Five months later.
 C. One year after discovery.
 D. One and one-half years after discovery, with no change in the polyp.

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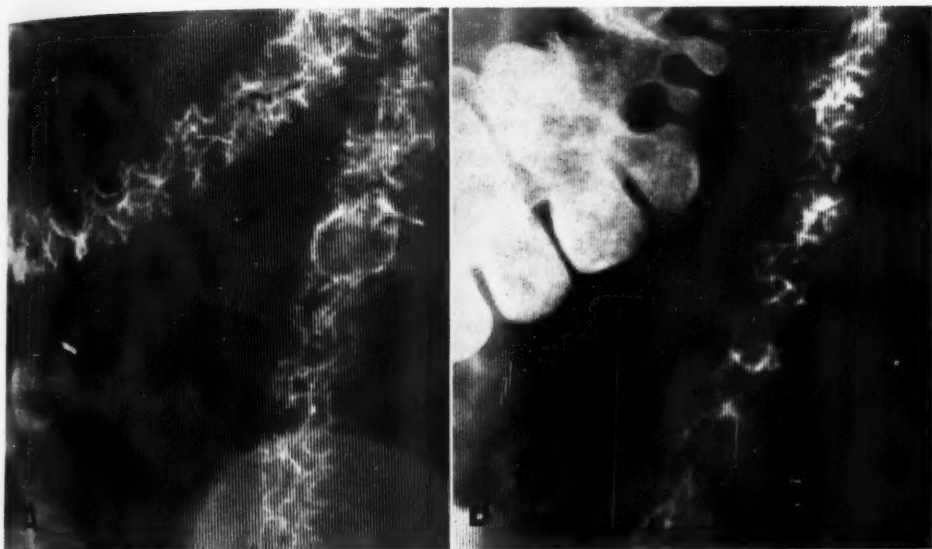


Fig. 9. Spontaneous passage of polyp.

- A. Polyp of descending colon. This polyp was twice shown in later studies.
 B. Study after one and a half years, showing that the polyp has disappeared.

occur in the first decade of life. In the period of time covered by our study (1946 to 1959) 420 postmortem examinations were performed in this hospital in the same age group and 4 of these disclosed unsuspected polyps in the colon. None of the charts recorded the passage of blood per rectum.

Several other children, not included in this series, gave a history of passage of bright red blood, with normal barium-enema examinations. On sigmoidoscopy, a small ulcerated area of the mucosa was found and was felt to represent the base of a polyp which had spontaneously sloughed. On 3 occasions a colonic polyp was recovered by the parent from the stool and identified microscopically.

Eight children were found to have a single colonic polyp above the reach of the sigmoidoscope and in these the bleeding was minimal. Because colotomy for removal of polyps is not without hazard, these children have been followed closely by serial barium-enema examinations, without operation. In 3 cases polyps were passed spontaneously, while 5 patients are still under observation, with 2 of these showing

mucosal intussusception. No significant change in size of the polyps has been seen in the examinations which extend over two years. Figure 8 illustrates a polyp which has been followed for one and a half years, associated with a small mucosal intussusception. In the 3 patients in whom the polyp was thought to have passed spontaneously, no change in size occurred prior to the final examination when the polyp could no longer be found. One of the children was followed for one and a half years before the fifth examination when the polyp was not seen (Fig. 9). Further work will be necessary to evaluate the interesting findings of Andrén and Friberg (1), who followed 2 patients in whom the polyp seemed to recede in size spontaneously.

Polyp searches represent less than 20 per cent of the barium-enema studies performed by us and on no occasion has a colonic polyp been found accidentally. At the same time, the inaccuracy of the simple barium-enema examination with a single filling and evacuation must be recalled. Mallam and Thomson (7) stated that in 19 per cent of children rectal bleeding was

caused by polyps of the colon. Our observations on over 400 postmortem examinations and approximately 700 barium-enema studies suggest that the incidence of undetected or unsuspected colonic polyps is low. Spontaneous passage by auto-amputation at the pedicle is the probable method of disappearance.

SUMMARY

Polyps of the colon in children can be accurately diagnosed from radiographs displaying the entire mucosa of the colon. This is achieved by serial fillings of the colon until evacuation is complete, followed by immediate films. The experience of The Montreal Children's Hospital over a fourteen-year period is reviewed. Observations on mural intussusception induced by colonic polyps, mucosal intussusception, spontaneous passage of polyps, and the incidence of unsuspected polyps in postmortem material are presented and discussed.

ACKNOWLEDGMENTS: We wish to thank Miss M. J. Miles for her secretarial work, Miss J. Cox for help with illustrations, and Dr. H. T. Davenport for his thorough reading and criticism of the manuscript.

SUMMARIO IN INTERLINGUA

Diagnose Radiologic de Polyps Colonic in Juveniles

Al Hospital Montreal pro Juveniles, 151 juveniles con polypos colonic esseva studiate in le curso del dece-quattro annos ab 1946 a 1959 incluse. Sex retornava plus tarde, supponemente con nove polypos, de maniera que un total de 157 examines esseva effectuate.

Esseva trovate que in juveniles un accurate diagnose de polypos del colon pote esser effectuate a base de roentgenogrammas que exhibi le complete mucosa colonic. Tal roentgenogrammas es obtenite post repletiones del colon con un mixtura de barium, aqua, e acido tannic, repetite serialmente usque le vacuation del intestino es complete. In le curso del ultime anno del presente studio, 22 polypos esseva trovate e solmente duo esseva mancate. Ambe istos esseva micre e situate in le recto. Es

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Montreal Children's Hospital
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opinate que illos haberea etiam potite esser trovate con un plus complete vacuation del colon.

Le major criterio del diagnose es le demonstration effective del polypo. Le recognition de un pediculo es un utile indication del natura del lesion. Esseva incontrate intussusception del complete spissitate del pariete intestinal o etiam—minus communemente—del tunica mucose sol.

Auto-amputation del polypo (con vacuation spontanee) pare haber occurrite in 3 casos.

Le revista de un serie de plus que 400 reportos necroptic e de 700 studios a barium (pro varie indicationes)—omnes concernente patientes de comparabile etates—suggereva que le incidentia de non-suspecte polyps del colon in juveniles es basse.

Comparison of Radioisotope Scanning with Cerebral Angiography and Air Studies in Brain Tumor Localization¹

JOHN G. McAFEE, M.D., and DAVID R. TAXDAL, M.D.

IN THIS PAPER, cerebral scintillation scans in 400 brain tumor suspects are evaluated and compared with the results of conventional neuroradiologic methods. Although the scanning technic has been applied to the diagnosis of intracerebral lesions for many years, it has failed to gain widespread use as a diagnostic tool (6). The opinion of the pioneer workers in this field differed widely on the clinical value of the procedure. There was almost uniform agreement, however, that scanning instruments could be greatly improved. Those developed for thyroid and hepatic lesions proved disappointing for cerebral lesions. Coincident scanners for positron-emitting nuclides reached a high degree of development at an early stage (3) but failed to gain popularity because of their complexity and expense.

During the past ten years, steady progress has been made in the development of scintiscanners. The detailed requirements for a satisfactory instrument will be published elsewhere. At the present time, commercial units are becoming available which fulfill most of these requirements and will be suitable for cerebral scanning. The essentials of good instrumentation are: (1) a scintillation detector with high sensitivity, adequate shielding and collimation, (2) a highly stable gamma spectrometer, and (3) a photographic display of the scanning image. Sodium iodide (Tl-activated) crystals, 2 3/4 inches in diameter and 1 3/4 inches thick, are readily available and have sufficient sensitivity for cerebral scanning with reasonably low doses of radionuclides. The crystal and photomultiplier tubes must be surrounded by 1 1/2 to 2 inches of lead for adequate shielding from the relatively high body background. A multichannel focusing lead collimator 3 inches in depth is

mounted below the crystal. For the best possible resolution, pulse height analysis must be used in the counting system. The spectrometer used for this purpose must have a high degree of stability. So-called "medical" spectrometers, which lack stability of their high-voltage supply, have proved to be inadequate.

The scanning image may be displayed on paper by a solenoid tapper which receives pulses from a scaler. A photographic type of presentation, however, greatly aids in the interpretation of intracerebral lesions. The eye can appreciate the small differences in count rate in cerebral scans as a change in film density better than as a difference in spacing of uniform dots on paper.

METHOD OF PROCEDURE

Once the necessary equipment is available, the actual procedure of cerebral scanning on patients is simple. The usual radioisotope used is I¹³¹-labeled serum albumin; 2.5 microcuries per pound of body weight (5.5 μ c/kg.) are injected intravenously twenty-four to forty-eight hours prior to the scanning procedure. The maximum dose used is 500 microcuries, regardless of the patient's size. Lugol's solution (0.5 c.c.) is given orally two hours prior to the injection of the isotope, in order to block the thyroid uptake of free I¹³¹ iodide.

The scans are performed with the patient recumbent on an x-ray table. Anterior and both lateral projections are used routinely. The detector moves at a speed of 5 to 6 inches per minute and advances 3/16 of an inch at the end of each line. In patients with suspected posterior lesions, scanning is also performed from the posterior projection of the head. Following each projection, a routine radio-

¹ From the Departments of Radiology and Neurosurgery, Johns Hopkins Hospital, Baltimore, Md. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

graph of the skull is obtained before the position of the head is changed. Each scan requires about twenty-five to thirty minutes for completion. A radiographic skull holder helps to keep the head immobile for this length of time. Agitated patients and children under four years usually require sedation.

Technically satisfactory scans have been performed in all age groups, even in infants of four weeks.

THE NORMAL CEREBRAL SCAN

In the photographic type of presentation, on regular x-ray film, areas of increased count rate are represented by film darkening. The film density to count rate relationship is usually so arranged that a slight increase in count rate (approximately 200 cpm) produces a considerable increase in the degree of blackening of the film.

Following the intravenous injection of the radioactive-labeled protein, the tissue within the body which contains the lowest concentration is the nervous tissue of the brain and spinal cord, because of the so-called blood-brain barrier. Thus, in the normal lateral scan (Fig. 1, A) the brain appears as a light area or "hole in the head" surrounded by structures with higher activity (increased darkening). A peripheral margin of activity is seen outlining the circular contour of the head, due partly to the vascular structures of the scalp. This peripheral activity gradually increases in thickness from front to back, due to the gradual widening of the superior sagittal sinus immediately underlying the calvaria. At or immediately behind the vertex, there may be a rather sudden widening of the peripheral activity, due to the entrance of large superficial cerebral veins into the superior sagittal sinus. When localizing markers are placed on the vertex, nasion, inion, and external meatus in the lateral projection, there is normally a marked increase in the activity beneath a line joining the nasion and external meatus. This line may be either straight or slightly convex. The increased activity

is chiefly due to the temporal muscles. On comparison of the two lateral projections, it is normally quite symmetrical. A marked or localized difference in contour is usually indicative of a space-occupying lesion at the base of the skull. The normal activity behind and below a line from the external meatus to the inion is quite variable in pattern. It is frequently asymmetrical in the two lateral projections in normal individuals, usually due to a larger lateral dural sinus on the side of greater activity. Because of this normal asymmetry, interpretation of posterior fossa lesions in the lateral projection is difficult.

In the anterior projection (Fig. 1, B), the normal brain tissue again appears as a central area of low activity with a margin of increased activity due to the scalp. In the midline, extending downward from the vertex, there is frequently an extension of increased activity due to the midline vascular structures. Below the level of the markers on the superior orbital margins and nasion there is a uniform increase in activity due to the muscles of the orbits and face, the vascular mucous membranes of the nasal fossae and sinuses, the tongue, and muscles of the neck. With voluminous frontal sinuses, irregular and occasionally asymmetrical activity may extend above the level of the superior orbital margins.

In the posterior projection (Fig. 1, C), the normal activity at the base of the skull is usually in the form of an inverted "V," extending upward on either side from the external auditory meatus to a point at the inion. Normally, in both anterior and posterior projections, the appearance is usually quite symmetrical; a careful comparison of one side to the other is most important for the detection of localized lesions. If the scans have been performed in a slightly oblique position, however, the normal structures will appear asymmetrical. The superimposition of the scanning images upon the accompanying radiographs obtained before the head is moved will avoid errors in interpretation due to faulty

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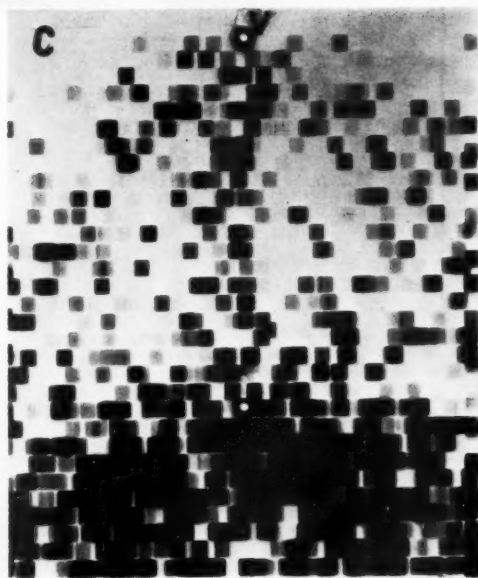
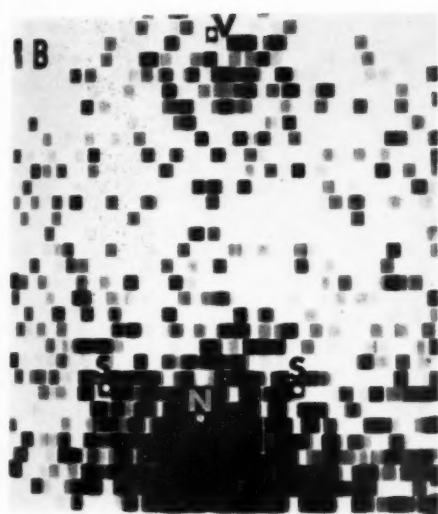
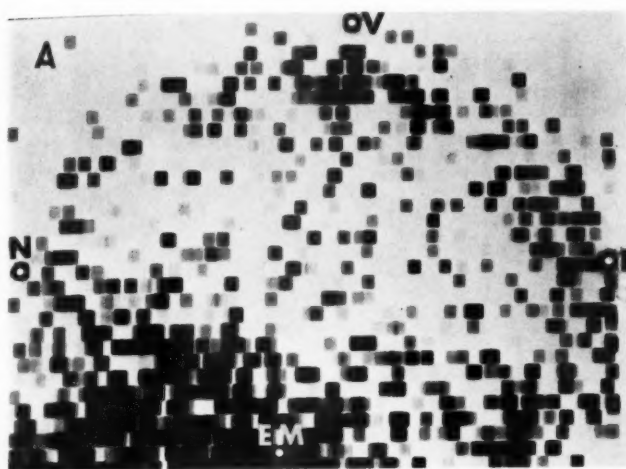


Fig. 1. Normal cerebral scintiscans.

A. Lateral projection. The central areas appear light, due to the low activity in the normal brain. A rim of activity in the scalp structures outlines the periphery of the head. The temporal muscle activity extends below a line from the external auditory meatus to the nasion. Irregular areas of activity due to occipital muscles are seen postero-inferior to a line from the external meatus to the inion. Localizing markers: V. Vertex. N. Nasion. I. Inion. EM. External auditory meatus. S. Superior orbital margin.

B. Anterior projection. Note the midline activity below the vertex, due to the central vascular structures, and the increased activity below the levels of the superior orbital margins and nasion.

C. Posterior projection, showing a midline vertical stripe of increased activity due to the superior sagittal sinus. The occipital muscle activity extends upward and medially on either side to a point in the midline at the inion. Note the symmetry of anterior and posterior projections from side to side.

positioning or to unusual anatomical variations of the skull.

In all projections, the peripheral margin of the head and the normal areas of increased activity along the base of the skull

should be clearly outlined. If these structures have to be artificially drawn on the scanning image before interpretation, the resolution of the scanning system is probably poor.

TABLE I: RESULTS OF CEREBRAL SCINTISCANS IN 350 FOLLOW-UPS ON 400 CONSECUTIVE PATIENTS

	Scan Positive	Scan Negative
Seventy-one Proved Brain Tumors		
Meningioma	13	0
Metastases	16	3 (posterior fossa 1)
Glioblastoma	5	2 (posterior fossa 1)
Astrocytoma	4	3
Glioma, Unspecified	4	2 (pontine)
Medulloblastoma	0	1 (posterior fossa)
Hemangioblastoma	0	1 (posterior fossa)
Acoustic Neuroma	1	0
Ependymoma	1	0
Pituitary or Suprasellar	4	6
Histology Uncertain	4	1
All Tumors	52 (73%)	19
Sixteen Positive Scans Without Brain Tumors		
Encephalomalacia	7	
A-V Fistula	3	
Hematoma, Intracerebral	2	
Abscess	1	
Orbital Granuloma	1	
Epilepsy	1	
Paget's Disease	1	

INTERPRETATION OF LOCALIZED LESIONS

In the presence of brain tumors and other intracranial masses the normal blood barrier or selective permeability of the cerebral vascular system breaks down, allowing the injected radioactive albumin to enter the tumor bed. The labeled material usually reaches a concentration of ten to twenty times the concentration of normal brain tissue and may occasionally become as high as one hundred times. With current techniques, areas of normal brain tissue on the scan frequently show small localized areas of increased count rate, due merely to statistical variations of the disintegration rate. In order to interpret an area of increased activity as a significant sign of an underlying lesion, it is necessary to identify a corresponding area of increased activity in three adjacent lines of the scan, and also to observe a corresponding area of activity in another projection. When a discrepancy is encountered in two opposing projections, a repeat scan will usually supply the definitive information necessary for a proper interpretation.

DIAGNOSTIC ACCURACY FOR INTRACRANIAL TUMORS

Follow-up results in the series evaluated here were similar to those reported by Shy *et al.* (4) and Sweet and his associates (5).

In our group of 400 patients suspected of having localized intracranial lesions, studied over a period of two years, a total of 423 examinations were performed, 23 of which were repeat studies. No means were used for selecting patients; referrals from internists, neurologists, and neurosurgeons of the institution and from neighboring hospitals were studied. Patients admitted as an emergency, however, and requiring immediate craniotomy and decompression could not be examined by this method.

In the follow-up of these 400 patients, 50 had to be excluded from further consideration because the presence or absence of a localized lesion was not established by surgery, neuroradiologic procedures, or by the subsequent clinical course. The results of the studies on the remaining 350 patients are summarized in Table I. In 257 patients subsequently proved to have no localized intracranial disease, there were no false positive diagnoses by scintillation scanning. In 6 patients, there was good clinical and radiologic evidence of intracranial tumor without histologic proof; in 5 out of 6, the scans were positive. In a group of 71 patients the presence of an intracranial tumor was established at surgery or necropsy. In 52 of these (73 per cent) the diagnosis of a localized intracranial lesion was made by scanning. Cerebral angiography was carried out in 43 of the 71 patients, and a lesion was correctly localized in 30 (70 per cent). The angiogram was completely negative in 7 instances, was unsatisfactory due to spasm in 2; a shift of the anterior cerebral artery without localization was demonstrated in 3. In 1 arteriogram, the tumor was not visualized because the middle cerebral artery branches in the area were incompletely filled. In 10 of the 71 proved tumors, localization of the lesion was made by scanning and not made by arte-

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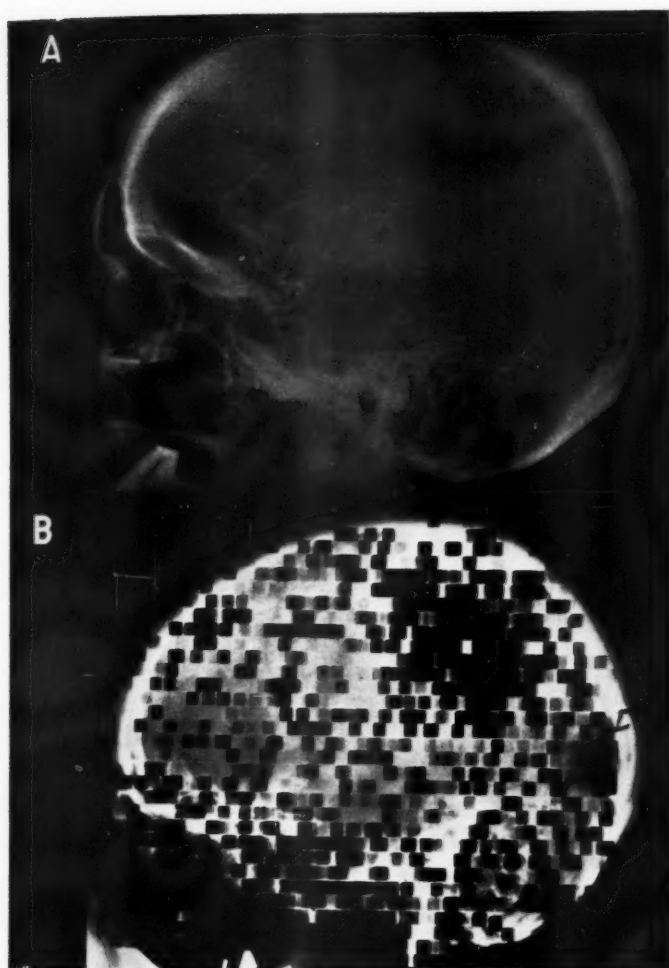


Fig. 2. Left parietal meningioma. Forty-one-year-old white female with headache of two years duration, homonymous right inferior quadrantic field defects, and loss of strength in the right hand.

A. Lateral carotid arteriogram, showing slight depression of the posterior parietal artery. A slight tumor stain was seen on a later film.

B. Left lateral scan superimposed on radiograph. A marked, localized increase in activity is seen in the left parietal region.

riography. Four of these lesions were metastatic, 2 were meningiomas, and 2 gliomas. On the other hand, 7 tumors were demonstrated by arteriography and missed by scanning. These 7 cases included 3 pituitary adenomas, 1 suprasellar cyst, 1 unspecified glioma, 1 astrocytoma, and 1 thalamic tumor. With the combination of scanning and arteriography, a total of 62 cases out of 71 were correctly diagnosed.

Only 21 pneumoencephalograms or ventriculograms were obtained in the group of 71 patients with proved brain tumors. Five of the 21 studies failed to indicate a localized intracranial mass. In 4 of the 5 (2 meningiomas, 1 temporal glioblastoma, 1 temporoparietal metastasis), localization was accomplished by scanning. Conversely, 6 tumors were demonstrated by air studies which were not detected by scanning. Two of these were pontine

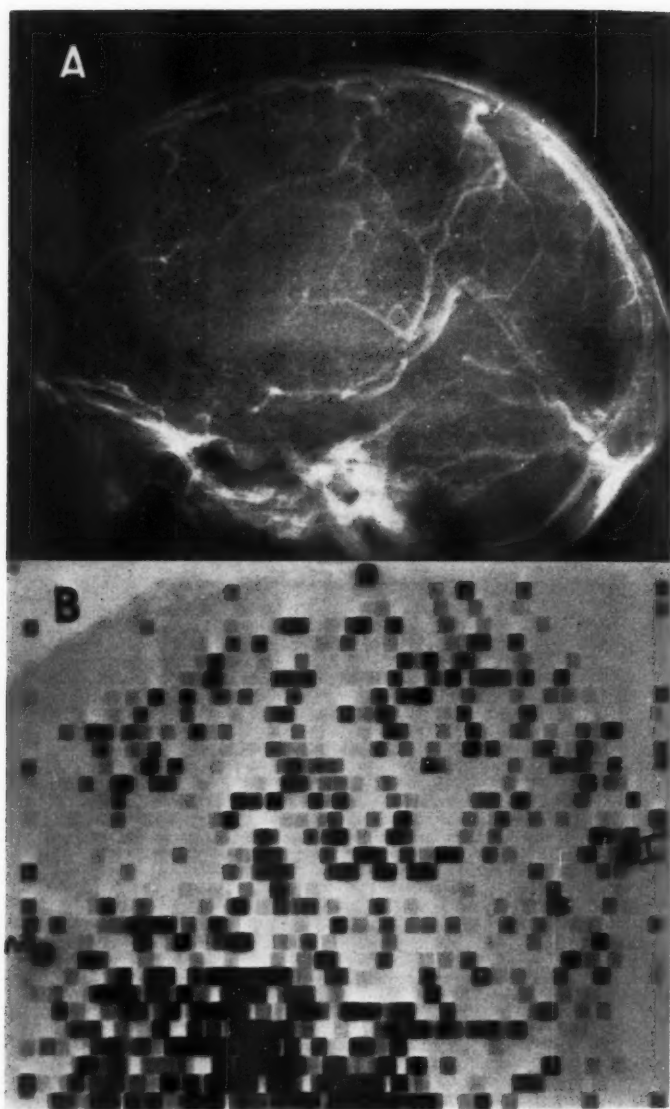


Fig. 3. Meningioma. Sixty-one-year-old white female with focal seizures of the right face for one year.

A. Lateral carotid angiogram, venous phase. An avascular spherical mass is outlined by the displaced superficial cerebral veins. The arterial phase showed only minimal displacement of the sylvian arteries.

B. Left lateral scan. An abnormal localized area of increased activity in the temporoparietal region. The increase in the count rate in the tumor bed is slight, compared with Fig. 2.

tumors, 2 cerebellar, 1 thalamic, and 1 was a frontal lobe cystic astrocytoma.

Abnormalities were apparent on plain radiographs of the skull in 24 of the 71 patients with proved tumors. Abnormal

calcification was seen in 11, expansion of the sella in 9, pineal shift in 5, localized destruction in 2, and hyperostosis due to meningioma in 3. In 1 patient, an infiltrating temporoparietal glioblastoma was

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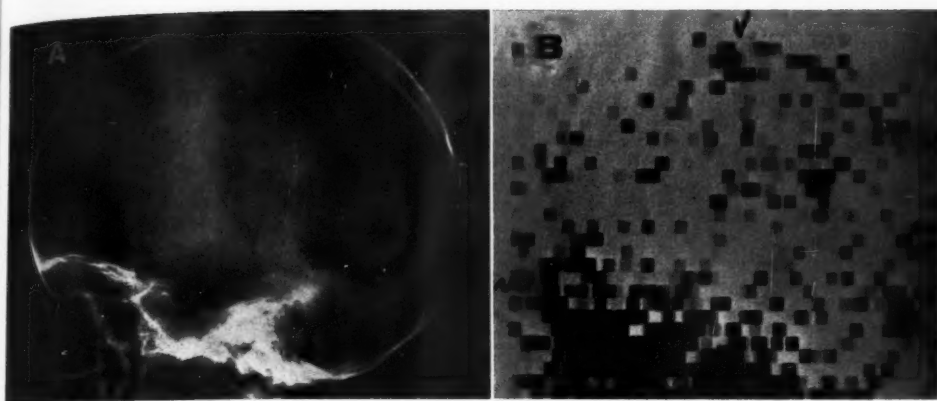


Fig. 4. Residual left occipitoparietal ependymoma. Nine-year-old Negro female. The large tumor was incompletely excised six years previously. Postoperative irradiation (tumor dose 4,500 r in five weeks) resulted in excellent clinical improvement.

A. Lateral skull film. Calcification of the tumor gradually developed following irradiation.

B. Lateral scintiscan. Only a minimal localized increase in activity remains in the tumor bed.

missed by scanning, arteriography, pneumoencephalography, and electroencephalography, but was discovered at craniotomy.

From Table I, it is quite apparent that certain histologic types of intracranial tumor are much better demonstrated than others by the scanning method. The diagnostic accuracy is highest for meningiomas, because these tumors concentrate the radioactive material to a high degree. Most metastatic lesions and gliomas of the cerebral hemispheres can also be readily diagnosed. Cellular astrocytomas are usually visualized, but 3 Grade I astrocytomas with cysts and areas of gliosis were completely missed on scans, even though the tumors were huge. In the astrocytomas with positive scans, there was a marked discrepancy between the actual size of the tumor and the relatively small area demonstrated by scanning; the cystic portions of the tumor were not shown (Fig. 6). Similarly, other intracranial encapsulated cystic lesions, such as suprasellar cysts, were not demonstrated.

The location of intracranial tumors is also an important factor in their detection by scintiscanning. Intracranial tumors were not demonstrated, unless they extended into the temporal fossa or considerably above the level of the clinoid

processes in the midline. Only 2 of 6 tumors of the posterior fossa were recognized by scanning and the only 2 pontine tumors in the series were missed.

In general, the estimate of tumor size and location determined from the scintiscan corresponded with surgical findings. In several instances, however, posterior frontal and temporal lobe sites were confused.

The breakdown of the blood-brain barrier in the tumor bed (the mechanism which determines whether or not a tumor is visualized on the scan) is not always related to the degree of vascularity or degree of malignancy. A majority of meningiomas have an extremely high activity (Fig. 2). A preoperative histologic diagnosis of meningioma cannot be made with certainty, however, on the basis of extremely high activity, because certain metastases and glioblastomas may have similar high levels. Furthermore, a minority of meningiomas will show only a slight increase in activity, apparently unrelated to histologic appearance (Fig. 3). The concentration of radioactivity within tumors cannot be explained entirely by the metabolic rate of the malignant cells, because many metabolically unimportant substances such as arsenate and versenate concentrate in tumors (1). The molecular

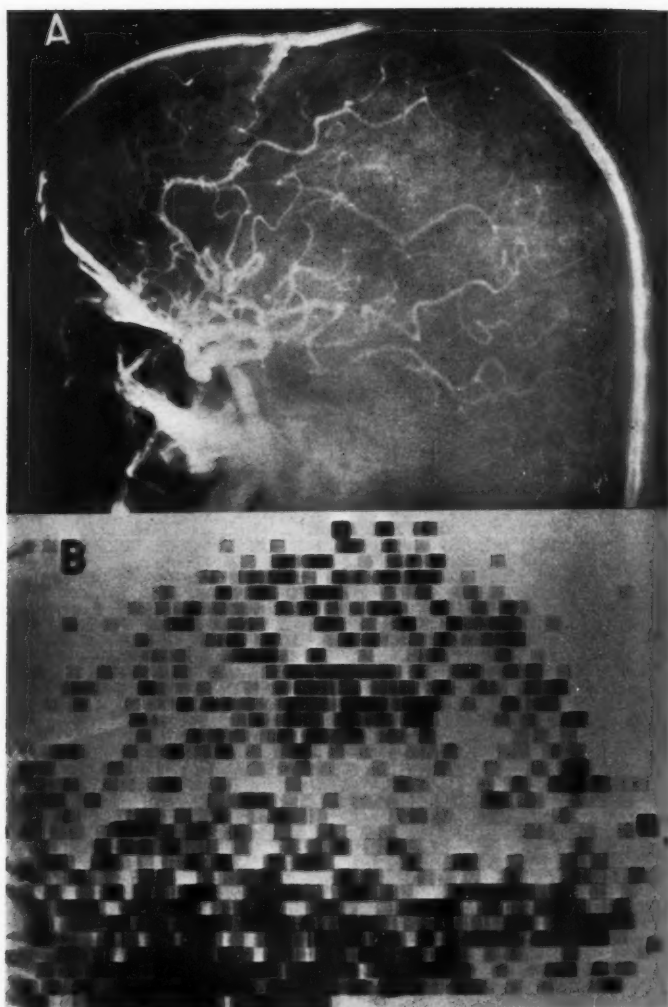


Fig. 5. Intracerebral metastatic carcinoma. Seventy-year-old white male with headaches, papilledema, and left hemiparesis for three months.

A. Right carotid angiogram showing some depression of the pericallosal artery, but otherwise normal.

B. Right lateral scintiscan. A large localized increase in activity is seen centrally. At surgery, the deep metastatic nodule was found to be very small but surrounded by a larger hematoma.

size of the labeled compounds appears to be an important factor in the degree of concentration within tumors. Necrotic areas and hematomas in the tumor bed usually concentrate the radioactive material to a high degree (Fig. 5). The authors have not observed a high uptake in edematous areas surrounding neoplastic tissues, as reported by Shy (4).

SCANNING ABNORMALITIES IN LESIONS OTHER THAN TUMORS

Sixteen patients in this series had definite localized areas of increased activity due to localized lesions other than neoplasms (Table I). Acute cerebral vascular accidents, less than one to two weeks in duration, may sometimes produce localized alteration of the blood-brain barrier as a

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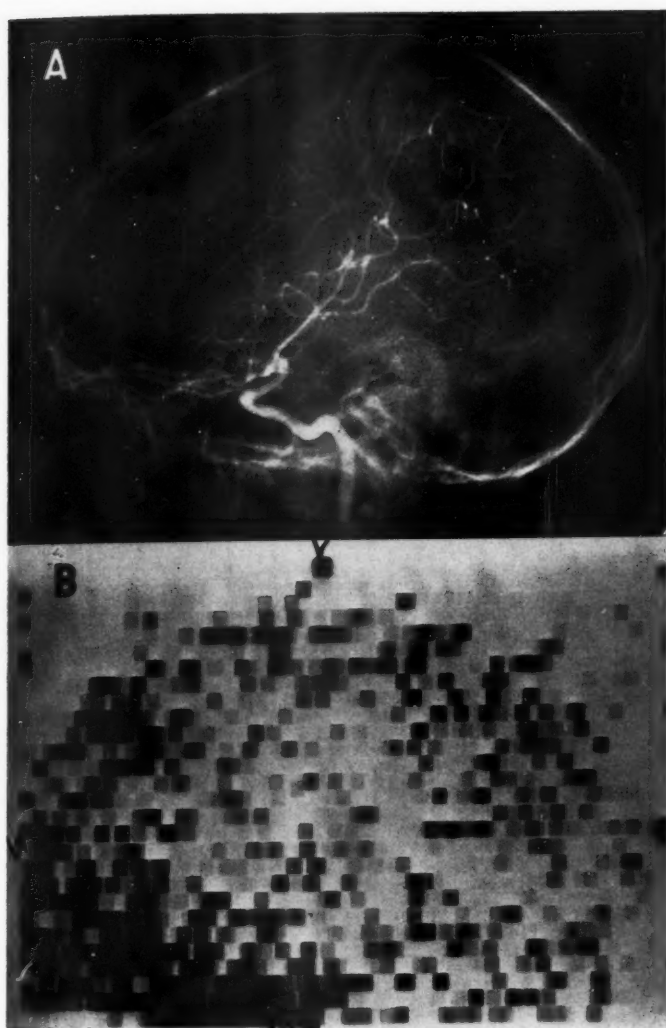


Fig. 6. Large cystic astrocytoma. Thirty-two-year-old white male with headaches for six months, papilledema, and prominence of right forehead.

A. Right carotid angiogram, showing marked postero-inferior displacement of the anterior and middle cerebral arteries by a large avascular frontal tumor. Note the localized erosion of the frontal bone. The anterior cerebral arteries showed a considerable shift to the left of the midline.

B. Lateral scintiscan. Only a small peripheral area of localized activity is seen in the proliferating portion of the tumor. The large cystic portions posteriorly are not visible.

result of either localized encephalomalacia (Fig. 8) or intracerebral hemorrhage. Many scans have been performed on patients with cerebral vascular accidents of several months duration and these have nearly always been negative. In one exception, a patient with localized en-

cephalomalacia of long duration had a craniotomy on the basis of a positive scan and a preoperative diagnosis of intracranial tumor.

Intracerebral inflammatory lesions have sometimes been detected by scintiscanning. Although one acute pyogenic abscess with

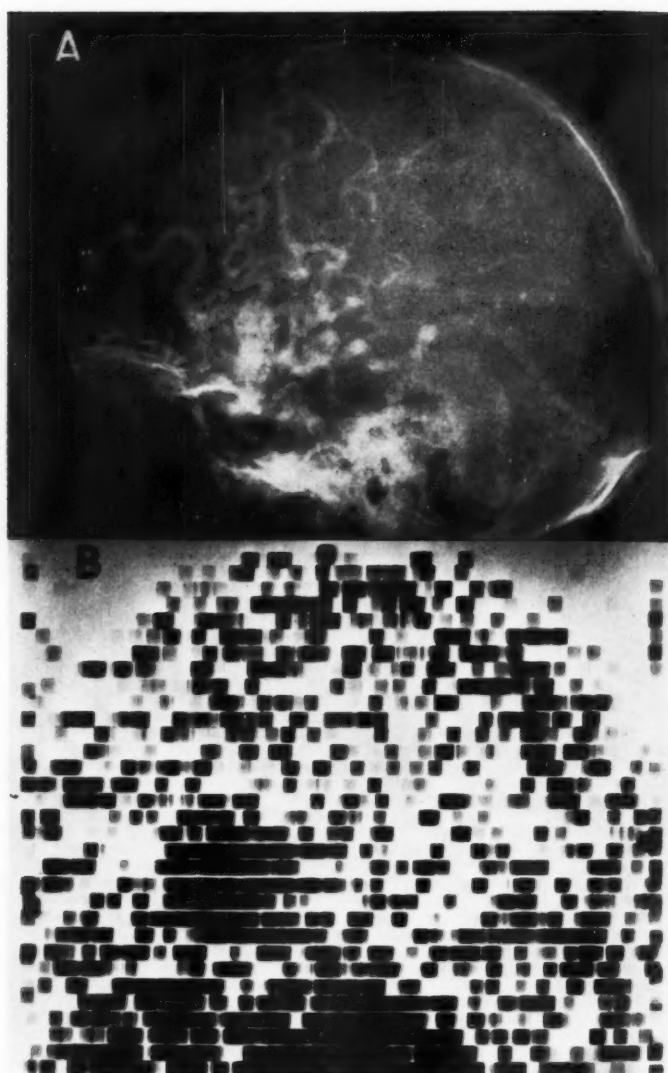


Fig. 7. Large arteriovenous fistula. Twenty-nine-year-old white male with syncopal attacks and psychomotor seizures for three years, without neurologic signs.

A. Right carotid angiogram, late phase. The large dilated vessels, chiefly at the base of the right frontal lobe and supplied by the anterior cerebral artery, drain into both superior sagittal and straight sinuses.

B. Lateral scintiscan. The localized areas of activity, chiefly in the inferior frontal region, correspond to the distribution of the abnormal vascular channels.

considerable necrosis was revealed by scanning (Fig. 9), another large and well encapsulated abscess of long duration was not discernible. One case of histoplasmoma (4) and one of tuberculoma (1)

have shown good radioisotopic concentrations. One patient of this series had signs of pansinusitis, unilateral papilledema, decreased vision, and slight proptosis. The clinical diagnosis was granuloma of

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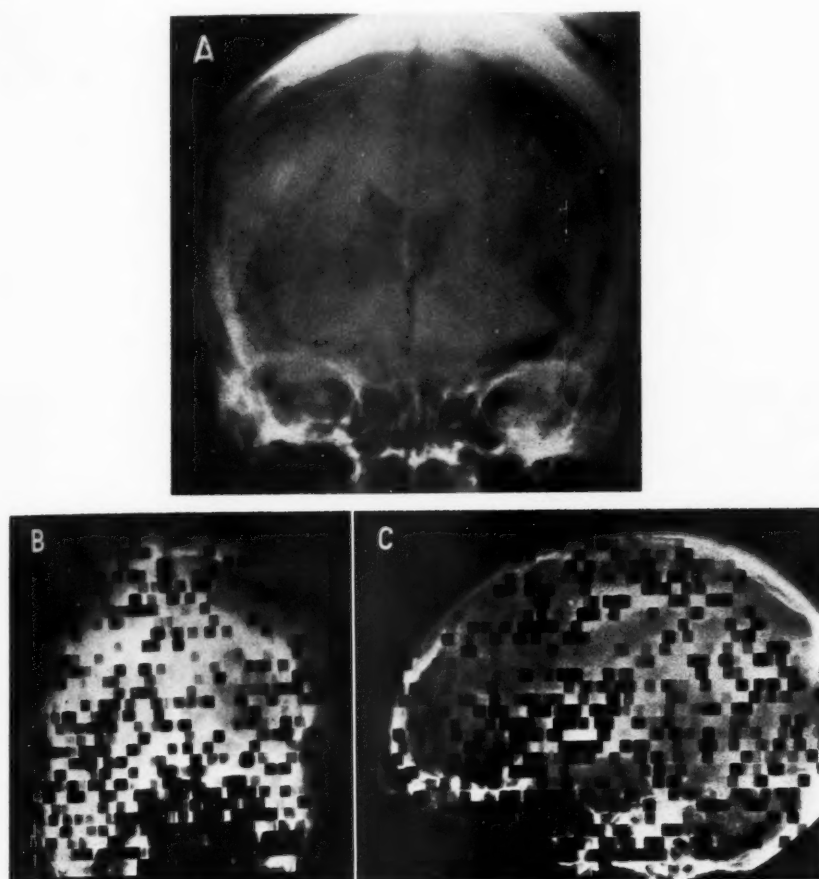


Fig. 8. Right frontal encephalomalacia. Forty-five-year-old colored male with left flaccid paralysis and left homonymous hemianopsia of recent onset.

A. Pneumoencephalogram normal except for slight asymmetry of the frontal horns. B and C. Anterior and right lateral scintiscans show abnormal localized activity in the inferior right frontal region, indistinguishable from an intracranial tumor. The carotid angiogram was normal. The neurologic signs improved after several weeks.

the orbit. The scan showed a localized area of increased activity posterosuperior to the normal orbital activity on the symptomatic side. Shy (4) reported a similar instance of orbital granuloma with a positive scan.

Hyperostotic lesions of the calvaria result in an abnormal increase in the thickness of the peripheral area of activity of the head, presumably due to the increased vascularity of the involved bone. Paget's disease of the skull may cause a widening of peripheral activity throughout

the entire calvaria in all projections (Fig. 10). In one instance, this disease obscured an underlying glioma on the scan. In one patient with marked hyperostosis frontalis, there was a corresponding slight increase in activity on the scanning image. In some meningiomas, part of the increased activity over the tumor area may be attributable to hyperostosis of the adjacent bony structures. This increased activity due to the hyperostotic calvaria may persist after the meningioma has been excised.

Many patients with idiopathic epilepsy

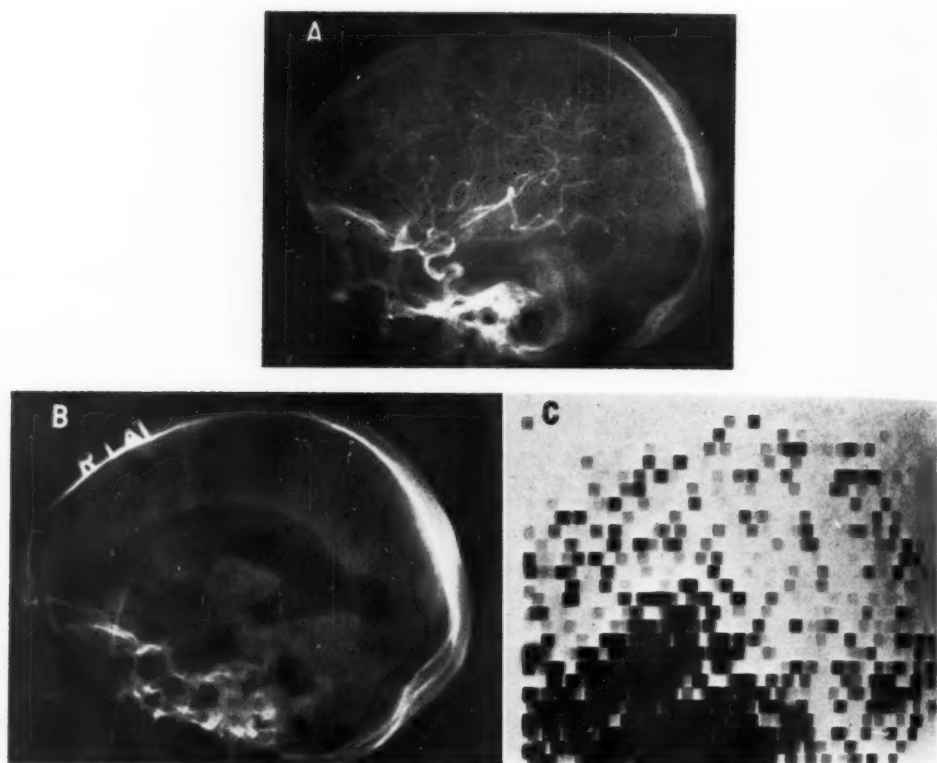


Fig. 9. Staphylococcal abscess of right frontal lobe. Sixty-two-year-old Negro female with three-month history of headache, drowsiness, progressive left hemiparesis, low-grade fever, leukocytosis, and lupus of the skin.

A. Right carotid arteriogram showing slight elevation of the basal portion of the anterior cerebral artery. There was minimal shift of this vessel in the frontal projection.

B. Lateral pneumoencephalogram. The frontal horn of the right lateral ventricle is foreshortened. There was no ventricular shift.

C. Lateral scintiscan showing a localized increase in activity at the base of the right frontal lobe merging with the normal temporal muscle activity. At surgery, the abscess was surrounded by extensive gliosis.

were scanned in this series. In all except one, the examinations were completely negative. In the single exception, a localized area with slightly increased activity was seen in the temporal region, associated with intractable temporal lobe seizures and hemiatrophy of the brain.

Any condition which temporarily alters the blood-brain barrier may produce abnormal areas of increased activity on scanning. Cerebral arteriography may alter the barrier on the side of injection for several days; because of this, cerebral scanning should precede arteriography whenever possible. Following an arteriogram, it is preferable to wait one week before performing a scanning procedure.

Air studies have reportedly altered the blood-brain barrier (2) and produced abnormal scans. In this series, several scans performed with residual air in the ventricular system have shown no evidence of abnormality; in one instance irregular areas with a slight increase in activity were apparently related to a preceding air study. Following craniotomy, large irregular areas with a marked increase in activity are usually seen, presumably due to operative trauma of the brain and increased vascularity of the overlying scalp. For several days following a burr-hole procedure, corresponding small round areas of increased activity can be seen peripherally in lateral and posterior pro-

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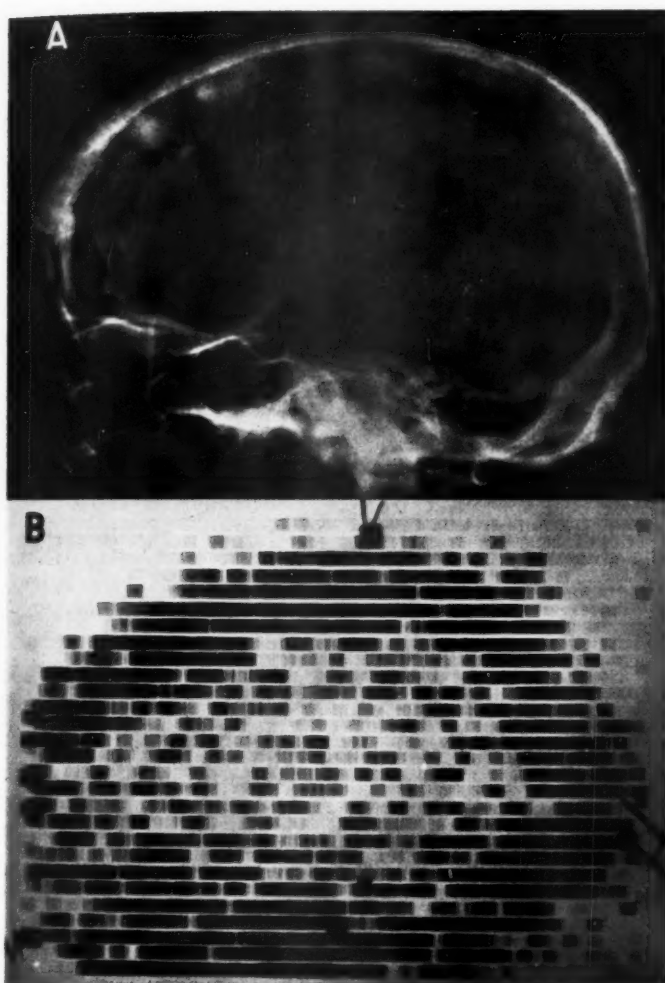


Fig. 10. Paget's disease of the skull.

- A. Lateral skull film showing diffuse hyperostosis of the calvaria.
B. Lateral scintiscan showing abnormal widening of the peripheral activity due to the increased vascularity of the involved bone.

jections. Two to three weeks following surgical procedures, the postoperative effects apparently disappear. Thereafter, the scans may be effectively used for evaluating the success of a surgical excision or postoperative irradiation therapy (Fig. 4). From animal experiments, extremely large doses of radiation (approximately 20,000 r) may alter the blood-brain barrier (1), but this has not been encountered with the usual dosage levels of clinical radiation therapy. Toxic states such as uremia,

hepatic coma, or drug intoxication may alter the blood-brain barrier (1), but alterations in cerebral scans from these conditions have not yet been described.

Although arteriovenous fistulas are usually demonstrated on scans as localized areas of activity (Fig. 7), the procedure is of no value in the detection of aneurysms of the intracerebral arteries. Several aneurysms were not discernible by scanning, one of which was an inch in diameter. Contrary to the experience of Sweet (5),

scanning was of no value in this series in the detection of subdural hematomas or hygromas. Similarly, a great variety of intracranial lesions failed to show any abnormal manifestations on scintiscans, including meningitis, post-meningitic subdural effusion, porencephalic cyst, aqueduct stricture, hypertensive encephalopathy, vascular or migraine headache, subarachnoid hemorrhage, pseudotumor syndrome, craniostenosis, glomus jugulare tumor, communicating hydrocephalus, and hypoparathyroid tetany.

In the initial studies of this series, several areas of localized increased activity were observed which were not reproducible and not constant in location with various projections. These false areas proved to be merely variations in count rate due to instability of the high-voltage supply and a shifting window of an unstable "medical" spectrometer.

POSITRON SCANNERS VERSUS CONVENTIONAL COLLIMATED SCANNERS

The coincidence scanner, used with positron-emitting nuclides— As^{74} or Cu^{64} , is able to detect an area of increased isotopic concentration within the skull at any depth with equal sensitivity. Both sides of the head are therefore scanned simultaneously in the lateral projection. Similarly, simultaneous scanning of anterior and posterior aspects is possible. The instrument therefore has the advantage of requiring only half the time for the total procedure.

There is considerable disagreement in the literature as to which instrument has better resolution, the positron scanner or the collimated scanner. Different workers have established different criteria (2, 3) and even different definitions of the term "resolution" as it applies to scintillation scanning. A series of experimental scans has been performed with spherical sources of various diameters in a 6-inch cube phantom, containing activities similar to *in vivo* activities in man. It has been found that the ability to detect volumetric sources for the two instruments is ap-

proximately the same. Thus, when a 1-inch source contains a concentration of radioactivity ten times that of the surrounding medium, it is detectable with either type of instrument. With the collimated scanner the source can be seen to a depth of 3 1/2 inches; this is sufficient for cerebral scanning, when opposing projections are used. With a collimated scanner, a 1-inch source containing only a 5:1 ratio is barely visible and then only if the source is close to the phantom surface. When the volumetric source is reduced to 1/2 inch in diameter, the ratio of concentrations between the mock tumor and brain has to be increased to 25:1 to be detectable with either instrument.

There are several practical disadvantages in using the commercially available positron scanner: 1. The cost of the equipment is more than twice that of commercial collimated scanners which are satisfactory for cerebral studies. 2. The positron scanner cannot be used for other diagnostic applications, whereas the collimated scanner may be employed for the diagnosis of thyroid, liver, splenic, renal, and mediastinal lesions (7). 3. The positron scanner has only a paper dot presentation, which makes the interpretation of small differences in count rate difficult, compared with a photographic presentation. 4. Positron-emitting nuclides are expensive compared with the readily available gamma-emitting nuclides. The cost of a typical patient dose of As^{74} arsenate, for example, is about ten times the cost of a typical dose of I^{131} serum albumin. 5. The sensitivity of a positron scanner is approximately one-tenth the sensitivity of a collimated sodium iodide crystal (2 3/4 × 1 3/4 inches). Much higher amounts of radioactivity therefore have to be administered, resulting in a higher total-body radiation dose. In a patient of average size receiving 5.5 mc/kg. of I^{131} serum albumin intravenously, the total body dose is approximately 0.6 rads. Workers with the commercial positron scanner have found it necessary to use a dose of 33 mc/kg. intravenously, resulting in a total-body dose of

about 4.2 rads. This relatively high dosage level prohibits scanning as a method for following the progress of a lesion. The radiation dosage with Cu^{64} versenate is much less. Its extremely short physical half-life and limited commercial availability, however, eliminate its possible use in daily clinical examinations.

A comparative study of the distribution of various radioisotopes in mouse ependymomas has been carried out by Dr. Gordon Long of the Neurosurgical Department of the Johns Hopkins Hospital. It has been found that the tumor-to-brain concentration ratios for As^{74} arsenate are inferior to those with either I^{131} serum albumin or the more recent compound Hg^{202} -labeled Neohydrin.

From the available data on human brain tumors, it would appear that histologic tumor types which concentrate I^{131} albumin will also concentrate As^{74} well; conversely, tumor types which concentrate one of these substances poorly, also concentrate the other poorly.

CONCLUSIONS

With the gradual rise in the absolute incidence of intracranial tumors, the need for a "screening" diagnostic method has increased. Cerebral scintiscanning fulfills this need, particularly for evaluating lesions of the cerebral hemispheres. It has successfully demonstrated over 70 per cent of all intracranial tumors. Its advantage over cerebral angiography and air studies is the complete freedom from complications and discomfort. The position and extent of intracranial tumors are usually portrayed accurately, because the tumor bed itself is visualized. Localization, therefore, does not depend on indirect signs of displacement of such normal structures as the contrast-filled cerebral vessels or the air-filled ventricles. In this series, the diagnostic accuracy has been much higher than for the only other non-traumatic diagnostic procedure—the electroencephalogram. The localization has been more precise, and there have been fewer false positive diagnoses.

Follow-up cerebral scans have proved useful for evaluating the course of patients with brain tumors, before and after surgical excision or irradiation.

The chief disadvantage of this procedure is that it is time-consuming for the patient and technician. On the other hand, it requires less of the physician's time than either air studies or cerebral angiography.

A localized area demonstrated by cerebral scanning almost always indicates a localized organic lesion. A positive scan, however, is not specific for intracranial neoplasm. Other confirmatory procedures should therefore be carried out before surgical exploration.

At the present time, the authors feel that the technic of cerebral scanning deserves a place in the evaluation of intracranial tumors equal to that of cerebral angiography and air studies. It should become a routine part of the investigation of brain tumor suspects following routine skull radiographs and preceding air studies or angiography. It supplements but does not replace the latter methods, chiefly because the detection is poor for encapsulated or cystic tumors, and for lesions of the brain stem and posterior fossa. Pituitary and suprasellar lesions are also frequently missed, but the majority of these are demonstrated on regular skull radiographs. Occasionally, the scanning method has successfully shown meningiomas, metastases, superficially spreading glioblastomas (4), and thalamic tumors when the other diagnostic techniques have failed. With the rapid advances in instrument design currently taking place, the clinical value of the procedure will be greatly enhanced in the near future.

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DISCUSSION

Giovanni Di Chiro, M.D. (Bethesda, Md.). At the National Institute of Neurological Diseases and Blindness, Bethesda, we have carried out 630 scans in brain tumor suspects. There are several points in which our experience differs from that of Dr. McAfee. One point I would like to stress is that the cystic astrocytomas have in our experience an increased uptake and are easily recognized. The slow-growing astrocytomas without cystic formations are, however, frequently missed and probably represent one of the limitations of the procedure.

Non-tumoral cysts (porencephalic), on the other hand, have a quite poor uptake. In fact, sometimes these non-tumoral cysts may stand out because of

their lower uptake compared to the surrounding tissue.

Dr. McAfee: It is of interest that at the Clinical Center of the National Institute of Health, with which Dr. Di Chiro is associated, the overall accuracy of scanning brain tumors has been quite similar to ours. These figures appear in the book by Shy on "Cerebral Scintillation Counting" (4).

I am glad Dr. Di Chiro brought out the fact that in astrocytomas sometimes the slow-growing tumors with a low grade of proliferation and areas of gliosis fail to show up on scanning. In addition to the areas of gliosis, we have not been able to demonstrate the cystic lesions of the astrocytomas.

SUMMARY IN INTERLINGUA

Comparation de Scintillo-Exploration a Radio-Isotopo con Angiographia Cerebral e Studios a Aere in le Localisation de Tumores Cerebral

Scintillo-exploraciones cerebral post injection de radio-isotopos (usualmente albumina serral marcate con I^{131}) esseva effectuate in 400 patientes suspecte de tumor cerebral. Le resultados esseva evaluatate in 350 casos in que le observationes de controlo posterior esseva adequate. In 71 casos, le presentia de un tumor intracranial esseva establite al chirurgia o al necropsia, e in 52 de istos le diagnose esseva establite per scintillo-exploration.

Le facto que le methodo es completamente libere de complicationes es un importante advantage in comparation con angiographia cerebral e studios a aere. In plus, le sito e le extension del neoplasma intracranial es usualmente delineate accuratamente, proque le spatio del tumor mesme es demonstrate.

Un localisate area demonstrate per scintillo-exploration cerebral indica quasi semper un localisate lesion organic. Un resultado positive, nonobstante, non es pathognomonic pro neoplasma intracranial. Altere investigationes confirmatori,

per consequente, deberea esser interpretate ante le institution de exploration.

A iste tempore, le autores opina que le technica del scintillo-exploration cerebral merita un placia in le evaluation de tumores intracranial equal a illo del angiographia cerebral e de studios a aere. Illo deberea devenir un parte routinari del investigation de casos suspecte de tumor cerebral, post routinari radiogrammas cranial e ante studios a aere e angiographia. Illo es un supplemento sed non un reimplacimento de istos, principalmente proque illo es paucio efficace in le detection de tumores incapsulate o cystic e de lesiones del pedunculo cerebral e del fossa posterior. Lesiones pituitari e suprasellar escappa etiam frequentemente al detection per le hic discutite methodo, sed le majoritate de illos es demonstrate per radiographia cranial regular. Occasionalmente le methodo del scintillo-exploration ha succedite a demonstrar meningiomas, metastases, glioblastomas in expansion superficial, e glioblastomas quando le altere technicas diagnostic se habeva provate inefficace.

Cerebral Angiostratigraphy: First Practical Results¹

P. ROCCA, M.D., and G. ROSADINI, M.D.

THE LIMITATIONS of the standard angiostratigraphic procedures with the classical projections, and even with supplementary views (oblique and under-the-chin-bregmatic), led us to devise a technic whereby the intracranial vascular system could be demonstrated at various levels simultaneously. This technic, which has been described in an earlier publication (1), permits dissociation of the different components of the intracranial vessels, freed from confusing superimposed shadows. With a single injection of contrast material, not exceeding in amount that used in standard stratigraphy (10 c.c.), projections of several layers of the cerebral circulation are achieved simultaneously. The advantages of such a procedure are apparent, since repeated injections of the medium for demonstration of individual layers, such as would otherwise be required for this purpose, are obviously out of the question. With the new technic, five stratigrams can be obtained, separated from one another by a distance of 1.0 cm., either in the anteroposterior or lateral projection.

From a preliminary study of normal subjects, it was evident that simultaneous angiostratigraphy would permit the demonstration of any vascular alterations, canceling out possible superimposed vascular or osseous shadows and affording more exact stratigraphic parameters than would otherwise be possible. On this assumption, we employed the procedure in a number of cases, immediately following standard arteriography, making use of the same injection.

The present paper reports our first practical results, indicating that our expectations were justified. While in some cases of malformation with a rich vascular component (glioblastoma multiforme and

metastatic tumors) the information contributed did not appear to extend beyond the limits of iconographic curiosity, merely adding some data of marginal interest to the basic angiographic picture, in other instances of expansive lesions with a particular vascular structure the findings were of considerable interest. This was true of some saccular aneurysms, voluminous angiomatous masses, and calcified tumors whose structures and relationships were decisively clearer and sometimes unexpected.

From our limited number of cases we have selected 2 of particular interest.

CASE REPORTS

CASE I: G. G., twenty years of age, gave a negative family history. At the age of six he had first exhibited mental symptoms. These were followed by generalized convulsions, sometimes with a jacksonian onset, on the left. These attacks had increased progressively in frequency until they occurred daily. At fourteen years the patient was hospitalized and an exploratory temporoparietal craniotomy was done, without disclosing anything of significance. This operation was followed by a right hemiparesis, which was progressive. Speech difficulties appeared, and the convulsive seizures continued with little decrease in frequency. About two months prior to admission to our institution the patient was found to have obvious symptoms of intracranial hypertension, with violent headaches, nausea, and vomiting.

Examination on entrance to the hospital revealed marked right spastic hemiparesis, with exaggeration of the deep reflexes and a positive Babinski test, on the right, as well as incoordination of both right extremities. Routine laboratory examinations were normal. Electroencephalography showed an area of slow waves in the frontal lower region on the left. A roentgenogram demonstrated a voluminous calcification in the left temporal region as well as evidence of the earlier craniotomy. Some dysarthric disturbances and a global intellectual deficiency of medium degree, with manifestations of irritability and intolerance, were also present.

Routine carotid angiography showed a pronounced shift upward of the group of sylvian vessels. In the

¹ From the Institute of Radiology, University of Genoa (Director, Prof. A. Vallebona), and the Neurological Department, San Martino Hospital (Chief Physician, Prof. G. Campailla), Genoa, Italy. Accepted for publication in January 1961.



Fig. 1. Case I. Standard cerebral angiogram: lateral projection, showing a wide discontinuity in the parieto-temporal region, result of a previous craniotomy; presence in the temporal region of an opaque mass having a calcareous aspect and very clear outlines. Good filling of the internal carotid with displacement upward of the sylvian group of vessels. Some vascular branches are projected, in their terminal tract, on the opaque mass.

Fig. 2. Case I. Cerebral angiostratigram: lateral projection. The vessels of the sylvian circulation can be seen, but the deep vessels are cancelled out. The opaque mass in the temporal region shows a noncalcified central nucleus having a peripheral calcareous coating. It is, beside, possible to observe that some small vessels belonging to the sylvian group extend into the mass.

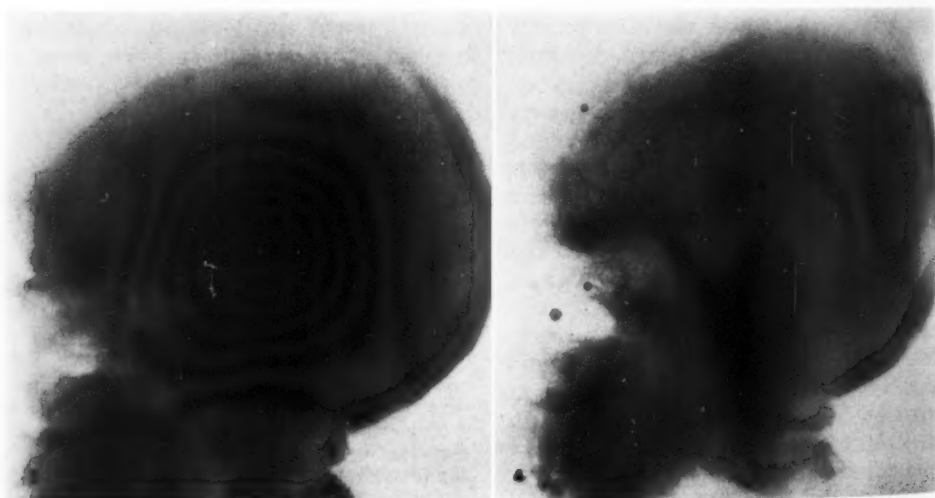


Fig. 3. Case I. Next deeper layer. On the posterior pole of the opaque mass a vascular net is well visualized showing the terminal branches of two small vessels of the sylvian group reaching the opaque mass and mingling with the terminal branches of a vessel on a deeper layer.

Fig. 4. Case I. A still deeper layer, showing the initial tract of the anterior cerebral artery as well as of the ascending polar anterior artery. There is clear visualization of a vessel which arises from the internal carotid, takes an anteroposterior rectilinear course, reaches the opaque mass, and at the posterior pole divides into a certain number of terminal branches. These enter into the mass, follow a medium-lateral course, and reach a more superficial layer to mingle with the terminal branches of the two small vessels coming from the sylvian circulation, visualized on the first stratigrams.



Fig. 5. Case II. Standard vertebral angiogram in lateral projection. Visualization of a wide angiomatous formation extending to all the posterior and occipital parietal region, which is injected by the vertebral technic. The vascular images of the large angiomatous formation, represented on the same plane, are superimposed.

Fig. 6. Case II. Deeper layer. The vascular images of the angiomatous formation visible on this layer, owing to the cancellation of those of the superimposed lower and upper layers, appear very clear and well defined in all their course.

lateral view (Fig. 1) small arterial branches could be seen projected in their terminal tract on the calcareous mass, without the possibility of their dissociation from the mass in the anteroposterior view. There thus remained a question as to the diagnosis—whether we were dealing with an avascular calcareous formation, as a calcified abscess, or a neoplastic process with partial calcification.

Sagittal angiostratigraphy showed first that the opaque mass in the temporal region was not completely calcified, as it appeared on the standard roentgenogram, but consisted of a noncalcified central nucleus surrounded by an intensely calcified outer rim. It was further found on examination of the successive stratigraphic layers that the mass was well vascularized, especially in its posterior aspect. In fact, those vascular branches which on the standard stratigram appeared to be directed toward the mass and were projected upon its image without any evidence to indicate whether they were intrinsic or extrinsic to the mass were seen to be intrinsic. At the level of the posterior pole of the tumor was a region of rich vascularization where the vessels coming from the superficial branches were entangled with those arising in the deep layers, thus insuring a double flow of blood to the mass (Figs. 2-4).

These observations allowed us to exclude a calcified abscess and to arrive at a diagnosis of neoplasm with a calcareous capsule. Operation (Prof. L. Perria) and histologic examination confirmed the diagnosis, showing an oligodendroglioma with a calcified margin. The tumor was removed and the

patient was discharged, clinically recovered, after an uneventful postoperative course.

CASE II: G. F., aged twenty years, gave a negative family and early history. A year previously there had developed left temporoparietal headache, with paresthetic sensations on the entire right side. Eight days before admission the patient had been hospitalized elsewhere because of a sudden meningeal hemorrhage. On transfer to our institute, a right hemiparesis was present, with slight deep hyperreflexia but no other significant signs. The usual laboratory examinations of urine and blood showed nothing abnormal. Cranial roentgenograms demonstrated a slight increase in the digital impressions. Electroencephalography disclosed irregularities in the background rhythm and the presence of slow waves in the left temporoparietal-occipital region. Left carotid angiography showed a wide angiomatous formation in the frontoparietal region. Vertebrobasilar angiography by the posterior percutaneous technic showed that the vascular malformation involved also the posterior region of the hemisphere.

Angiostratigraphy performed immediately supplied morphologic data of considerable interest. With elimination of the superimposed images of the lower and upper layers, it was possible to demonstrate at different levels the extension of the vascular field fed by the basilar artery. On the stratigram at average depth a large triangular formation representing a voluminous vascular lacuna was visualized, which on the standard angiogram had been ob-

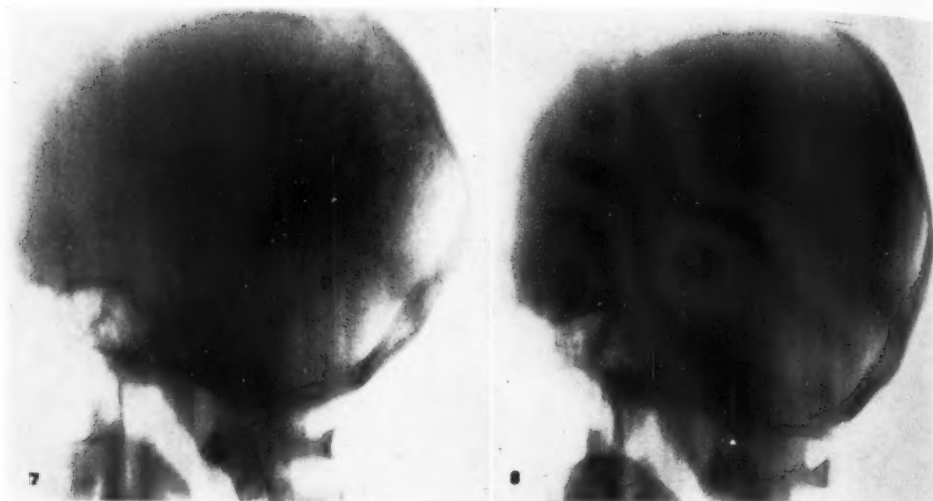


Fig. 7. Case II. An even deeper layer. Beside the clear visualization of the vascular images of the arterial branches on this layer, we have clearly visualized an image of triangular form, with well defined outlines and homogeneous opacity, representing a vascular saccular dilatation.

Fig. 8. Case II. Medial layer. On this stratigram—because of the medial situation of the layer under examination—all the vascular images are cancelled, owing to their position on more superficial layers.

secured by the superimposed shadows of other layers of the angioma. The angiostratigraphic study thus offered some new structural aspects of the malformation examined, besides exactly localizing it at different layers. The patient did not reach the operating table but was dismissed with medical therapy.

COMMENT

The pathological material so far available cannot permit absolute conclusions as to the exact value of this new complement to neurological investigation. We believe, however, that the first results are significant and we are encouraged to continue our studies with this technic. Beside showing new aspects of well known pathologic pictures, it can, in some cases at least, contribute information helpful in the intricate task of the neurosurgeon.

SUMMARY

Cerebral angiostratigraphy by a technic permitting simultaneous demonstration of the intracranial vascular system at different levels has proved of value in clinical use. Dissociation of the vascular structures, layer by layer, makes possible determination of their volume and estimations of their depth.

Two cases are reported. In one, standard angiography showed a calcareous mass in the temporal region, on which some branches of the arteries of the sylvian group were projected. By angiostratigraphy it was possible to exclude a calcified abscess and to diagnose an oligodendroglioma with a central noncalcified nucleus and a calcific capsule, into which the vessels of the sylvian group entered. The diagnosis was confirmed surgically.

The second patient had a parieto-occipital angioma. In this instance it was possible to demonstrate also a deep saccular dilatation which on the standard angiogram was obscured by overlying shadows.

It is believed that cerebral angiostratigraphy represents a diagnostic contribution of value, particularly in neurosurgical cases, when it can furnish useful information to the surgeon.

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SUMMARIO IN INTERLINGUA

Angiostratigraphia Cerebral: Prime Resultatos Practic

Angiostratigraphia cerebral—con le utilisation de un technica que permette le simultanee demonstration del systema vascular intracranial a differente nivellos—se ha provate de valor pro objectivos clinic. Le dissociation del structuras vascular—strato post strato—rende possibile le determination de lor volumine e estimationes de lor profundor.

Es reportate duo casos. In le un, angiostratigraphia standard monstrava le presentia de un massa calcaree in le region temporal. Brancas del arterias sylvian esseva projicite super illo. Per medio de angiostratigraphia il esseva possibile excluder le diagnose de un calcificate abscesso e

establi le diagnose de un oligodendroglioma con un non-calcificate nucleo central e un capsula calcific, con le vasos sylvian entrante in illo. Iste diagnose esseva confirmate chirurgicamente.

Le secunde patiente habeva un angioma parieto-occipital. In iste caso il esseva possibile demonstrar etiam un profunde dilatation saccular le qual—in le angiostratigraphia standard—esseva obscurate per superjacente umbras.

Es opinate que angiostratigraphia cerebral representa un contribution diagnostic de valor, particularmente in casos neurochirurgic ubi illo pote fornir importante informationes al chirurgo.



Congenital Hypoplasia of the Abdominal Muscles and Associated Genitourinary Tract Abnormalities¹

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CONGENITAL hypoplasia of the abdominal musculature is a rare but important affliction of children, first described in the German literature in 1839 by Fröhlich (2). The earliest reports in the English literature are those by Henderson in 1890 (5), Parker in 1895 (12), Guthrie in 1896 (4), and Osler in 1901 (11). Since that time over 100 cases have been recorded in the literature (1, 3, 6-10, 13, 14).

The appearance of the abdomen in these children is characteristic (Fig. 3). The abdominal wall is protuberant, flabby, and thin, with intestinal peristalsis often visible. There may be complete or partial absence of the abdominal muscles. Those of the anterior abdomen are most commonly involved, but the posterior muscles such as the quadratus lumborum may be affected. The flanks are bulging and the skin over the abdomen is wrinkled. While the disease is usually found in males and bilateral cryptorchidism is almost invariably present, several instances have been reported in females.

The often overlooked or unappreciated lethal aspect of the disease lies in the frequently associated urinary tract abnormalities. Hydronephrosis is present, the ureters are markedly dilated and tortuous, and the bladder is enlarged and hypertrophied. Bladder neck or outlet obstruction has been reported in approximately half of the cases, although in one series the incidence was 85 per cent (7). This may take the form of median bar hypertrophy, urethral valves, urethral pouches, urethral stenosis, or complete absence of a urethral orifice. These abnormalities lead to the problems of stasis, infection, and renal insufficiency. Uremia is the most frequent cause of death, and few patients live to be ten years old.

Other congenital malformations may be present. Anomalies of the gastrointestinal tract, which have been reported in 20 per cent of the cases (14), are often unsuspected and fatal. Anomalies of the extremities include congenital dislocation of the hip, metatarsus varus, and polydactylism. Cardiovascular and nervous system malformations are infrequently cited.

ETIOLOGY

The etiology of the urinary tract abnormalities remains obscure. There are several speculations, none of which have proved totally acceptable.

1. Stumme suggested that the primary defect is an outlet obstruction leading to bladder enlargement and secondary pressure atrophy of the abdominal muscles (15). This seems unlikely for the following reasons: (a) congenital absence of the muscles may be seen without any urinary tract abnormality; (b) outlet obstruction is often present without absence of abdominal muscles; (c) muscles may be absent which have never been in contact with the bladder; (d) an outlet obstruction has not been demonstrated in all cases with known hydronephrosis and hydroureter; (e) examination of the muscles seems to indicate that the primary process is not atrophy, but agenesis.

2. In 1901, Bardeen and Osler stated that the primary defect might be the aplastic abdominal musculature which offered no resistance to the expanding bladder so that complete micturition was not possible (11). This does not seem likely, since patients with omphaloceles do not have abdominal musculature yet their urinary tracts are normal, and, in fact, absence of the muscles may occur without urinary tract complications.

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TABLE I: SUMMARY OF CASES

Case	Sex, Race, and Age	Abdominal Muscles	Genitourinary Tract	Outlet Obstruction	Gastrointestinal Tract	Bilateral Cryptorchidism	Other Anomalies	Present Status
I: A. H.	M, W, 21 mo.	Partial absence	Bilateral hydronephrosis and hydroureters	+	-	+		Dead Age 11 yr.
II: G. D.	M, N, 17 mo.	Complete absence	Bilateral hydronephrosis and hydroureters	-	-	+	Patent urachus	Lost to follow-up
III: D. P.	M, W, 1 mo.	Complete absence	Bilateral hydronephrosis and hydroureters	?	Malrotation of gut	+	Polydactylism Pectus excavatum	Stable Age 4 yr.
IV: D. G.	M, W, 1 da.	Partial absence	Bilateral hydronephrosis and hydroureters	-	-	+	Bilateral metatarsus varus	Dead Age 3 days
V: F. H.	M, W, 2 yr.	Partial absence	Bilateral hydronephrosis and hydroureters	-	-	-	-	Stable Age 4 yr.
VI: F. W.	M, W, 6 mo.	Complete absence	Bilateral hydronephrosis and hydroureters	?	-	+	-	Stable Age 2 yr.
VII: M. N.	M, W, 12 da.	Complete absence	Bilateral hydronephrosis and hydroureters	+	-	+	Pigeon breast	Stable Age 1 1/2 yr.

3. The last major proposal, and the most reasonable to us, is that of Silverman (14). Between the fifth and tenth weeks of gestation the abdominal wall, the genitourinary tract, and the gastrointestinal tract are in a stage of development such that an insult at that time could produce the associated malformations. This insult could result in either structural or neurogenic abnormalities of the genitourinary tract, leading to hydronephrosis and hydroureter.

THERAPY

The treatment of children in the group under consideration centers around the genitourinary tract. Certainly malformations of the gastrointestinal tract should be looked for and corrected. The major therapeutic measures include support of the abdominal muscles with corsets or reconstructive surgical procedures to strengthen the abdomen and improve micturition. The second problem is obtaining satisfactory urine drainage, for which nephrostomy, cystostomy, and urethral catheterization have been used. Surgical correction of a bladder outlet obstruction may be undertaken. Greene feels that a vesical neck resection should be done even though the urinary stream is good and no outlet obstruction is demonstrated (3). Other surgical measures include ureteroplasty and uretero-ileo-neocystoplasty. Urinary tract infection, which is almost invariably present, necessitates the use of multiple and varied courses of antibiotics.

ROENTGENOGRAPHY

Roentgenologic manifestations of the disease are striking. The plain abdominal film reveals a flabby abdomen which appears out of proportion to the size of the thoracic cage and lies asymmetrically to one side. The bowel often contains a great deal of gas. Intravenous and retrograde urograms demonstrate unilateral or bilateral hydronephrosis. The ureters are markedly enlarged and tortuous, often resembling the colon in size. The bladder



Fig. 1. Case I: Cystograms demonstrated bilateral hydronephrosis, hydroureters, and a distended bladder.

is characteristically large, irregular in outline, and may have a projection which extends up toward the umbilicus. Tra-

beculation of the bladder may be a prominent feature. Cystography will usually verify the findings observed on intravenous urography, since ureteral reflux often occurs.

PRESENTATION OF CASES

Seven cases of absence of the abdominal muscles and associated urinary tract abnormalities have been seen at University Hospitals of Cleveland during the past ten years. No reports of the condition are available in the radiologic literature and, since the radiologist is often involved in the management of this problem, we are relating our experience with these 7 cases.

CASE I: A. H., a 21-month-old white male, was first admitted to University Hospitals on June 4, 1950, with recurrent fever. He had no anterior abdominal muscles below the umbilicus and bilateral cryptorchidism was present. Urine cultures grew out *A. aerogenes*. Intravenous urograms revealed a nonfunctioning left kidney and right hydronephrosis. Bilateral hydroureters were demon-

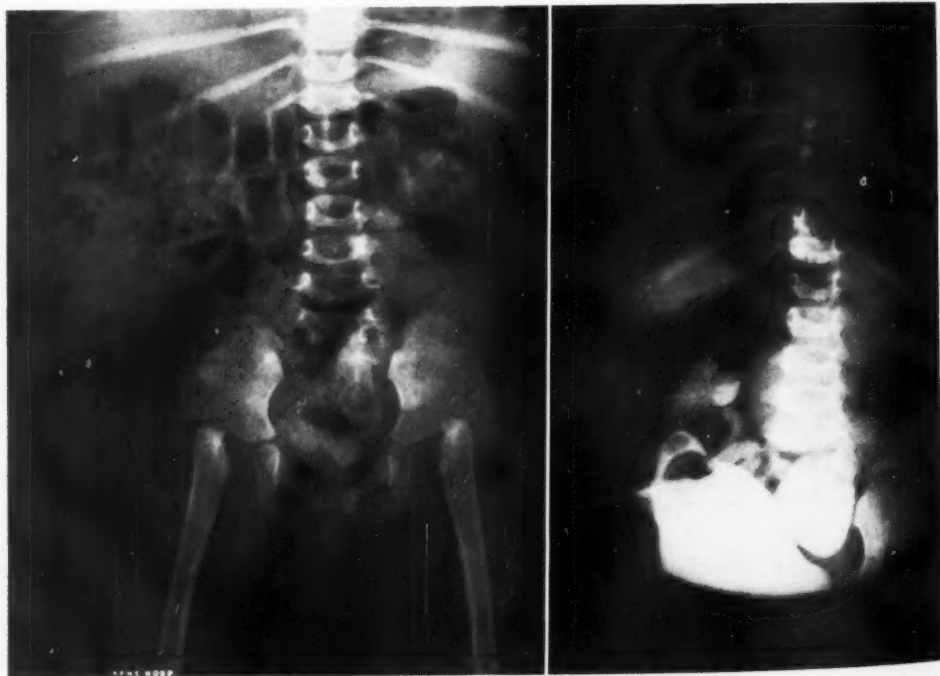


Fig. 2. Case II: A one-hour film from an intravenous urogram (left) shows poor excretion, hydronephrosis, and hydroureters, more marked on the left. Notice the asymmetrical abdomen and bilateral dislocations of the hips. Cystogram (right) done through a patent urachus confirms the presence of hydronephrosis and hydroureters.

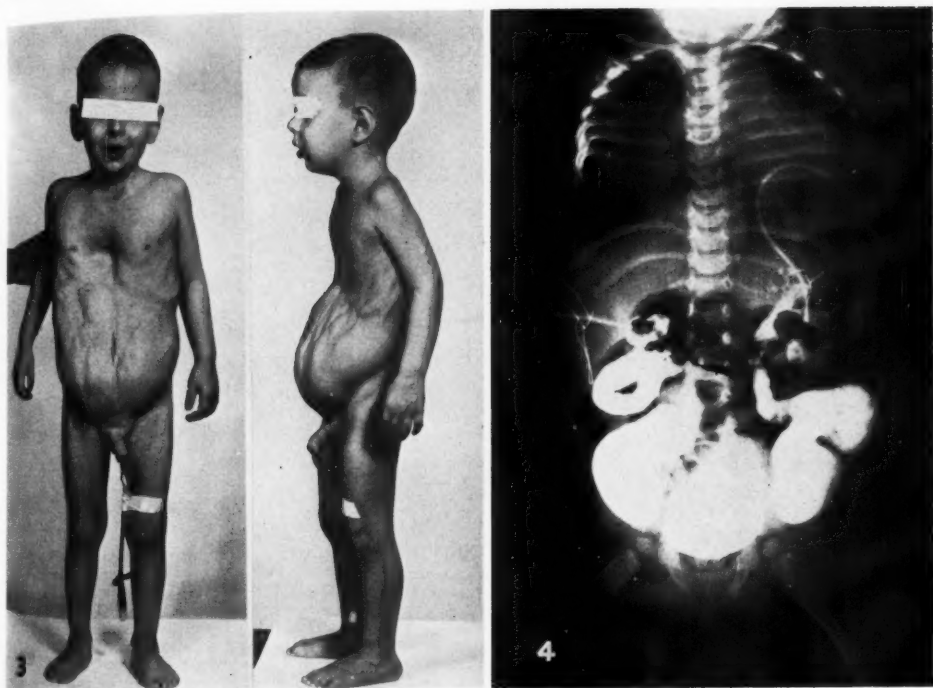


FIG. 3. Case III: Pictures taken when the patient was two and a half years old demonstrate the characteristic abdomen, pectus excavatum, and indwelling bladder catheter.

FIG. 4. Case III: Film of the abdomen taken on April 3, 1957, after the injection of the urinary tract through nephrostomy tubes demonstrates bilateral hydronephrosis and hydroureters.

strated by reflux during cystography (Fig. 1). Cystoscopy, on July 10, revealed chronic cystitis and an elevated median bar. Treatment was by antibiotics and constant drainage.

The patient was seen several more times for recurrent fever and abdominal pain. Surgical resection of the bladder neck on Dec. 1, 1950, was followed by improvement in the urinary stream and a decrease in residual urine. A second transurethral resection of the bladder neck was done on April 30, 1951, and a third on June 11, 1951. The child continued to have recurrent fever and chronic urinary tract infection, making constant catheter drainage necessary. In another attempt to eliminate this, a fourth resection was done on Aug. 21, 1954, without success. Renal function gradually deteriorated and death occurred in renal failure on Aug. 14, 1959. Post-mortem examination was not performed.

CASE II: G. D., a 17-month-old Negro boy, was first seen at University Hospitals on July 5, 1951, because of passing urine from his navel. The child had always voided through a patent urachus, having passed urine *via* the urethra on only three known occasions. He had had several hospitalizations elsewhere for urachal infection and was admitted for possible repair of the urachus.

On physical examination, the patient appeared

healthy. A patent urachus was present with surrounding cellulitis of the abdominal wall. Bilateral cryptorchidism and complete absence of the abdominal muscles were noted. An intravenous urogram revealed bilateral hydronephrosis and hydroureters, more marked on the left (Fig. 2). Bilateral dislocations of the hips were present. Surgical excision of the urachus was performed and a suprapubic cystostomy tube inserted. No obstruction of the bladder neck was identified. The dislocated hips were treated with closed reduction and spica.

During the next six months, the patient was hospitalized on several occasions for cast change, cystostomy tube change, and treatment of resistant urinary tract infection. Attempts at removal of the tube were unsuccessful because of dribbling and large residual urine. The patient was subsequently lost to follow-up.

CASE III: D. P., a month-old white boy, was first seen at University Hospitals on Sept. 4, 1956, with complete absence of the abdominal muscles, bilateral cryptorchidism, polydactylism with an extra digit on the left fifth finger, and pectus excavatum (Fig. 3). A cystogram and intravenous urogram revealed bilateral hydronephrosis and hydroureters. Bilateral injections of the upper urinary tract through nephrostomy tubes verified the bilateral

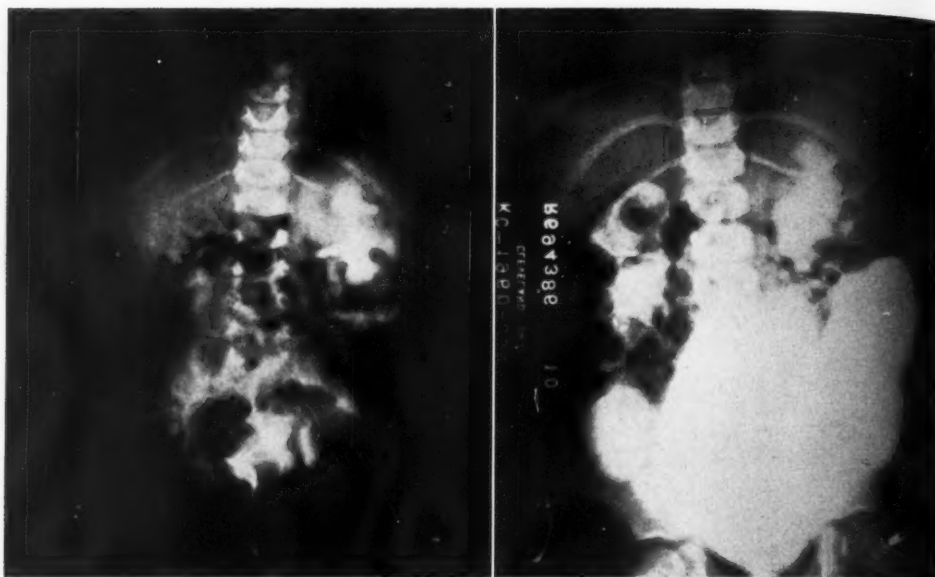


Fig. 5. Case III: An intravenous urogram (left), Sept. 30, 1957, after bilateral uretero-ileo-neocystostomy, demonstrates the left ileal segment (arrow). A cystogram (right), June 28, 1960, reveals marked interval dilatation of the ileal segments.

hydronephrosis and hydroureter (Fig. 4). On cystoscopy, a mild narrowing of the bladder neck was thought to be present. A repeat cystoscopy on April 3, 1957, was interpreted as showing no real outlet obstruction.

After the nephrostomies, the child did well with only one episode of fever. On April 8, 1957, the right ureter was excised and a uretero-ileo-neocystostomy was done without incident. On Aug. 15, a similar procedure was performed on the left side (Fig. 5). At surgery, an incomplete rotation of the gut was found and corrected. Meantime the child had done well with no evidence of urinary tract infection. Intravenous urograms showed good function on the left, poor on the right. The patient was maintained on catheter drainage and continued to do well, although urine cultures grew out *E. coli*. Renal function has remained relatively stable.

On May 4, 1959, a transurethral resection of the bladder neck was done for possible outlet obstruction. On the last admission in June 1960, the patient seemed to be in satisfactory condition except for persistent pyuria. There has been gradual dilatation of the transplanted ileal segments (see Fig. 5).

CASE IV: D. G., a one-day-old white boy, was admitted to University Hospitals on July 26, 1958. He was born at another hospital, where he was found to have complete absence of the abdominal muscles, bilateral cryptorchidism, and club feet. A barium-enema study was performed when masses were felt in the abdomen (probably enlarged ureters).

The colon perforated in the region of the sigmoid, and the patient was then transferred. Admission examination did not reveal clinical evidence of peritonitis.

An exploratory laparotomy was done on admission and the perforation of the sigmoid colon was repaired. A generalized meconium peritonitis was present, and the patient died suddenly the next day. Autopsy demonstrated marked bilateral hydronephrosis and hydroureters, the ureters averaging 1.5 cm. in diameter. The bladder was dilated, showing extreme trabeculation and hypertrophy of the muscles. The abdominal muscles were entirely absent with the exception of the left rectus. No outlet obstruction could be identified. Microscopic examination of the organs was unremarkable.

CASE V: F. H., a white boy of 2 1/2 years, was seen at University Hospitals on Feb. 22, 1959, with a history of the onset of gross hematuria six months previously. Work-up at another hospital at that time revealed bilateral hydronephrosis and hydroureters. On admission he appeared as a healthy, normally developed child in no acute distress. Over the left abdomen the muscles were absent except for the rectus. On the right, there was a defect in the right upper quadrant, but the remaining muscles apparently were present. No other anomalies were noted.

Laboratory data included a normal hemogram and urinalysis. The blood urea nitrogen was 16.5 mg. per cent. Intravenous urograms revealed bilateral hydronephrosis and hydroureter, more



Fig. 6. Case V: Cystogram illustrates a large asymmetrical bladder with left hydronephrosis and hydroureter. There is no reflux on the right.

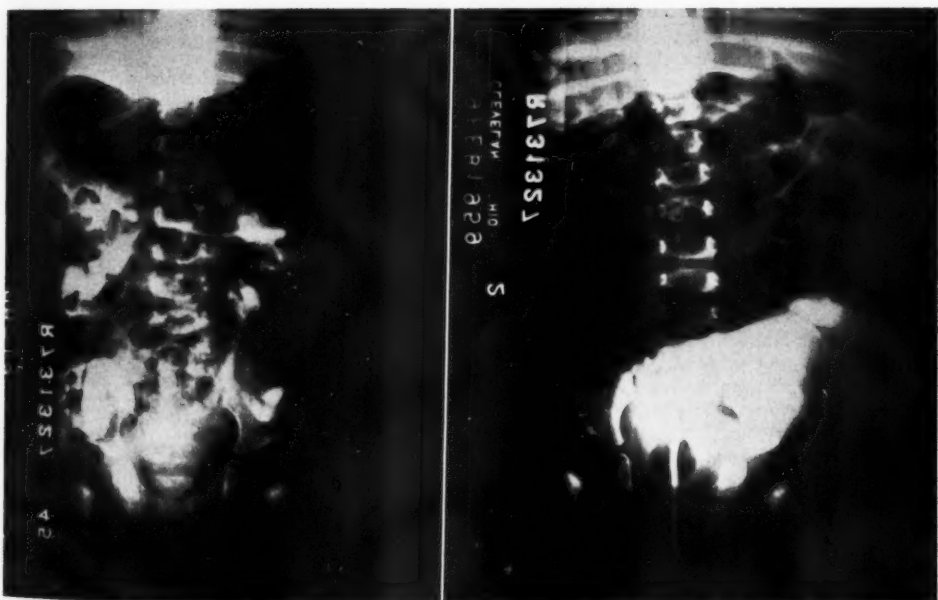


Fig. 7. Case VI: Intravenous urogram (left) shows bilateral hydronephrosis and hydroureters. Cystogram (right) demonstrates a large redundant bladder with no reflux into the ureters.

marked on the left. A cystogram demonstrated a large, irregular bladder with reflux up the left ureter (Fig. 6). Cystoscopy showed an atonic

bladder with no evidence of bladder neck obstruction. The residual urine was 1,000 c.c. The patient was discharged on constant catheter drainage with



Fig. 8. Case VII: At nineteen days of age the patient exhibits a distended abdomen with wrinkling of the skin. This appearance has led to the term "prune-belly syndrome".

the possibility of a wedge resection of the bladder at a future date. Since that time, he has continued to do well on constant drainage, and no surgical procedures have been performed.

CASE VI: F. W., a 6-month-old white male, was first seen at University Hospitals on Feb. 22, 1959, with a history of absence of the abdominal muscles since birth. The pregnancy and family history were unremarkable, and the child was in apparent good health, with normal growth and development. He was admitted to exclude urinary tract abnormalities. The only remarkable physical findings were complete absence of the abdominal muscles and bilateral cryptorchidism.

Blood studies revealed the following: Hemoglobin 12.8 gm., white blood cells 12,600, blood urea nitrogen 15.1 mg. per cent. The specific gravity of the urine was 1.015; it contained an occasional white blood cell and yielded no growth on culture. Residual urine was 30 c.c. Intravenous urography demonstrated bilateral hydronephrosis and hydroureters (Fig. 7). A cystogram revealed a large pear-shaped bladder with no evidence of ureteral reflux (Fig. 7). Cystoscopy at this time was unsuccessful.

The patient has since done well, with no urinary tract infection, voiding problem, or renal deterioration.

CASE VII: M. N., a 12-day-old white boy, was admitted to University Hospitals on April 22, 1959, for evaluation of absence of the abdominal muscles (Fig. 8). The preceding history was unremarkable. Physical examination demonstrated complete absence of the muscles of the abdomen, low-set ears, and bilateral cryptorchidism. Pyuria was present and urine culture grew out *E. coli*. Intravenous urograms and cystograms showed bilateral hydronephrosis and hydroureters.

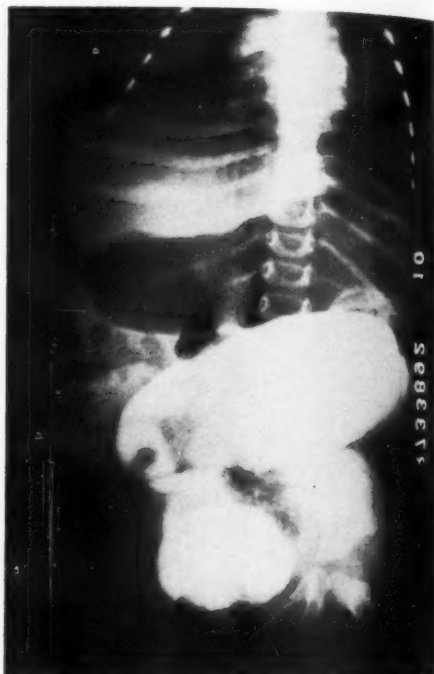


Fig. 9. Case VII: Cystogram illustrates a large abdomen with bilateral hydroureters. Notice the extremely large and tortuous left ureter.

Cystoscopy demonstrated an elevated posterior bladder neck and on July 1, 1959, this was resected. The bladder was dilated and the wall thinned. A suprapubic cystostomy tube was inserted. The child was discharged on constant drainage to be followed in the out patient clinic. He was last seen on June 13, 1960, for otitis media and urinary tract infection. His renal function had remained stable, with a normal urea clearance and blood urea nitrogen of 13.9 mg. per cent. He had been maintained on constant drainage. Repeat cystograms again demonstrated hydronephrosis and hydroureter (Fig. 9).

DISCUSSION

Our cases appear to follow the general pattern of those reported in the literature (Table I). All of the patients were males, with bilateral cryptorchidism (except for one instance), and had bilateral hydronephrosis and hydroureters. Other anomalies included patent urachus, pigeon breast, pectus excavatum, dislocation of hips, club feet, polydactylism and malrotation of the gut. No cardiovascular or neurological defects were encountered.

The etiology of the genitourinary tract

abnormalities remains unexplained. A definite structural bladder neck or outlet obstruction could be demonstrated in only 2 patients, 1 of whom had an elevated median bar and the other an elevated posterior bladder neck. Resection of the bladder neck was done in both cases, without improvement, and constant catheter drainage had to be continued. The observation of a hypertrophied bladder without evidence of structural outlet obstruction (Case IV) may lead to the speculation that a functional (neurogenic) obstruction was present.

The most important therapeutic problem has been the resistant urinary tract infection. This has best been controlled by eliminating stasis (cystostomy, nephrostomy, or urethral catheter) and with antibiotics. With control of the infection, renal function has in most instances remained stable or deteriorated slowly. Substitution of a section of ileum for a ureter did not apparently improve the final result in Case III, though renal function has remained stable. In general, efforts to reverse or correct the hydronephrosis and hydroureters have been unsuccessful. Any patient with hydronephrosis or hydroureter of unknown etiology should be carefully examined for hypoplasia of the abdominal muscles, either complete or partial.

The roentgenologic abnormalities are well demonstrated in the accompanying illustrations. Cystograms have, in our experience, offered certain advantages for examining and following the status of the upper urinary tract since: (a) they are easily done and do not require a venipuncture; (b) ureteral reflux is usually present; (c) visualization does not depend upon renal function; (d) voiding urethrograms may be obtained to determine outlet obstruction; (e) there is relatively less dilution of contrast material by residual urine and better visualization of the ureters and bladder is obtained. The gastrointestinal tract should be examined for unsuspected anomalies, although this was not done in our cases.

SUMMARY

The syndrome of hypoplasia of the abdominal muscles with associated urinary tract abnormalities has been briefly reviewed, and our experience with 7 cases has been presented.

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SUMMARIO IN INTERLINGUA

Hypoplasia Congenite del Musculos Abdominal e Associate Anormalitates del Vias Genito-Urinari

Hypoplasia congenite del musculos abdominal es un affliction rar sed serie de infantes. Le musculos pote esser completamente o partialmente absente.

Le condition occurre le plus communemente in masculos, e cryptorchidismo es quasi invariabilmente associate con illo. Anormalitates del vias urinari es frequentemente presente. Hydronephrosis occurre; le ureteres es dilatate e tortuose; le vesica es hypertrophiate. Obstruction del cervice o egresso del vesica se trova reportate in circa un medietate del casos. Anomalias del systema gastrointestinal e del extremitates ha etiam essite notate.

Le manifestationes roentgenologic de iste condition es frappante. Un pellicula regular indica un molle abdomine, in

disproportionation con le dimensiones del thorace e situate asymmetricamente a un latere. Le anormalitates del vias urinari es demonstrabile per urographia e cystographia. Le plus importante problema therapeutic es resistente infection del vias urinari. Es reportate septe casos.

Le autores ha trovate que cystogrammas es particularmente avantageose proque (1) illos es facile a effectuar e non require venepunctura, (2) refluxo ureteral es usualmente presente, (3) le visualisation non depende de function renal, (4) urethrogrammas in vacuation pote esser obtenite pro determinar le obstruction de egresso, e (5) le dilution del substantia de contrasto per le urina residue es relativamente minus marcate.



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Antral Deformity Due to Perigastric Adhesions or Bands Simulating Carcinoma of the Stomach¹

ABRAHAM GEFFEN, M.D., and FRIEDA FELDMAN, M.D.

PERSISTENT narrowing or deformity of the stomach is a frequent and difficult diagnostic problem, the difficulty lying in the differentiation between carcinoma and a benign lesion. Although the diagnostic criteria summarized by Golden (3) and by Kirklin (10) indicate with some degree of certainty the presence of gastric carcinoma, even the most experienced observer may at times find it hard to distinguish a benign from a malignant lesion in the antrum. Many authors have published well documented reports in which antral narrowing or deformity simulating carcinoma has been proved to be due to a benign condition, such as spasm, antral gastritis with or without gastric ulcer, or hypertrophic pyloric stenosis: Holsti (5), Serck-Hanssen (13), Jenkinson and Latteier (6), Jordan and Lahey (9), Cohn and Gold (1), Flood (2), Lundie, Scott, and Mackenzie (11) Pattinson, Osborne, and Tanner (12). These and other writers attest to the difficulty of differentiating benign and malignant changes in the antrum. The intention of the authors of this paper is not to discuss all types of benign antral lesions, but to consider only prepyloric deformity due to perigastric adhesions or bands simulating the change produced by gastric cancer.

REVIEW OF LITERATURE

Jenkinson and Hamernik (7), in 1948, and Jenkinson, Pfisterer, Norman, and Latteier (8), in 1952, were the first to call attention to the fact that perigastric adhesions and bands may simulate carcinoma of the stomach. The latter authors remarked in 1952 that very little had been written on the subject, and so far as could be discovered, no article has since appeared on this specific topic. Harris (4) in 1914

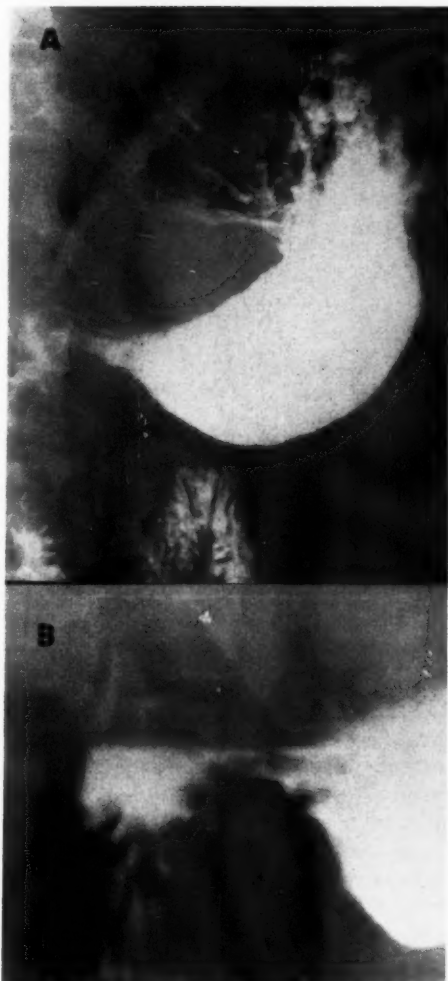


Fig. 1. Case I: Prone oblique view (A) and erect compression fluoroscopic film (B) showing narrowing of the prepyloric segment, sluggish peristalsis, interpreted as possible carcinoma. Exploratory operation revealed no intrinsic lesion of the stomach. The deformity was due to adhesions.

and Taylor (14) in 1922 had described deformities of the duodenum due to congenital bands with resultant obstructive

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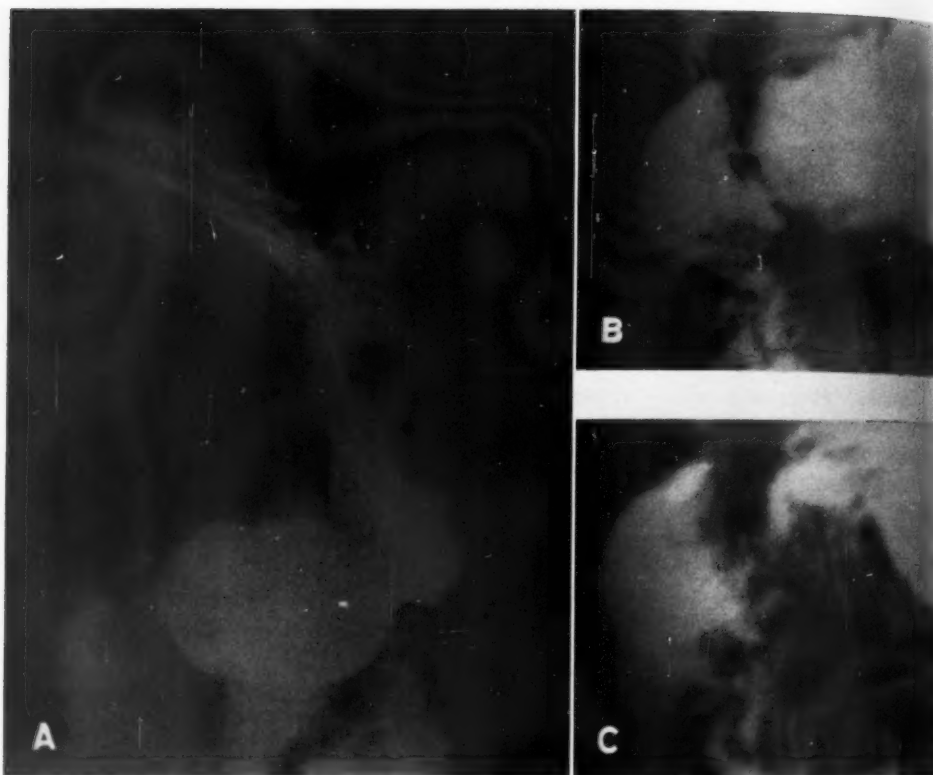


Fig. 2. Case II: Prone oblique view (A) and compression fluoroscopic films (B and C) show prepyloric deformity due to adhesions from previous operation for repair of perforated ulcer. Projection of barium, in the prone oblique view, simulating an ulcer crater was attributable to a pseudodiverticulum of pylorus resulting from the adhesions.

phenomena, although neither of these authors mentioned pyloric or antral deformity. Jenkinson *et al.* documented 7 cases of surgically proved perigastric adhesions and bands involving the pyloric antrum simulating carcinoma radiologically: 4 were congenital; 2 were post-cholecystectomy adhesions; and in 1, fibrosis and adhesions were related to a prepyloric ulcer. It was observed that both congenital anomalies and inflammatory adhesions are to be taken into consideration and that the pathology is dependent on developmental as well as on adult anatomic relationships.

Pattinson, Osborne, and Tanner (12) in 1959 reported 7 cases of benign lesions of the pyloric antrum simulating carcinoma, in 1 of which the antral deformity was due to adhesion of the gallbladder

or to fibrosis from a healed prepyloric ulcer, or both. There are thus 8 recorded cases of perigastric adhesions simulating cancer of the stomach.

CASE PRESENTATIONS

The senior author (A. G.) first became interested in this subject as a result of a mistake in the roentgen diagnosis of Case I.

CASE I: R. K., a 62-year-old female, was first admitted in August 1952, with a history of epigastric symptoms for two and a half years. Nine years previously she had undergone a cholecystectomy and appendectomy; twenty-eight years previously a hysterectomy. Barium-meal examination (Fig. 1) on Aug. 8 showed constant narrowing of the prepyloric segment of the stomach. This was interpreted as gastric cancer. Exploratory operation on Aug. 27 revealed no intrinsic lesion of the stomach; the antral deformity was found to be due to adhesions between the prepyloric region of

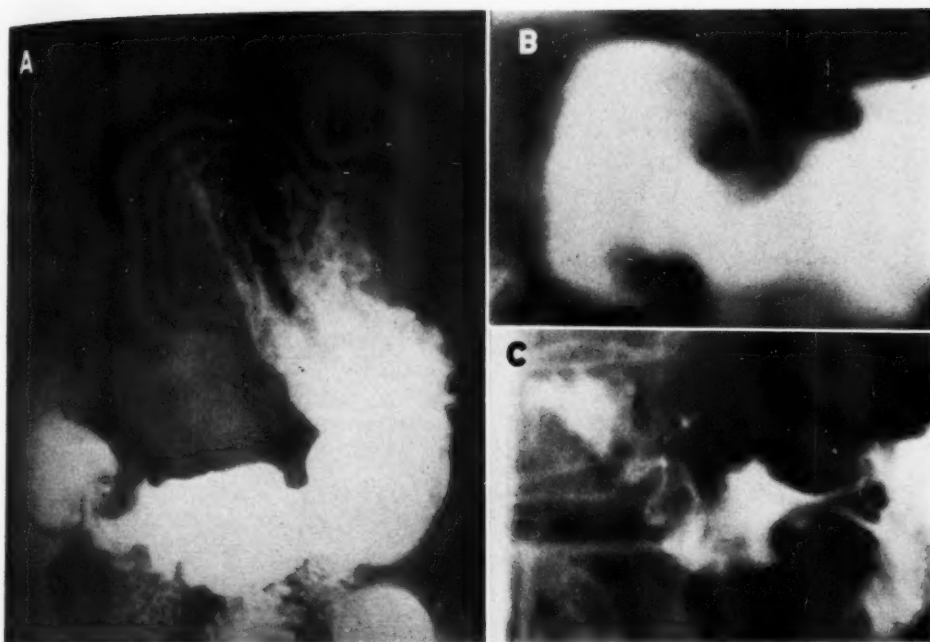


Fig. 3. Case III: Prone oblique view (A) and compression fluoroscopic films (B and C) showing narrowing, prominent folds with "pseudoulcer" crater, and poor peristalsis, interpreted as suspicious of gastric cancer. Exploratory operation revealed an omental band compressing the antrum; no intrinsic lesion.

the stomach and the undersurface of the liver and gallbladder bed.

CASE II: S. I., a 54-year-old male, was admitted in July 1954 because of acute onset of pain, weakness, and tarry stools. There was a nine-year history of duodenal ulcer and three years previously, a perforated ulcer had been repaired. A barium-meal study (Fig. 2) was interpreted as showing prepyloric deformity due to adhesions from the earlier operation. At surgery, a subtotal gastrectomy, adhesions, and scarring of the old duodenal ulcer were found, as well as a pseudodiverticulum of the pylorus, accounting for the prepyloric deformity.

CASE III: On March 18, 1959, A. K., a 70-year-old male, was admitted with clinical findings compatible with gastric cancer, which was also suspected on barium-meal examination (Fig. 3). An exploratory operation revealed an omental band compressing the antrum. There was no intrinsic abnormality of the stomach.

CASE IV: H. C., a 66-year-old male, was first seen in July 1955 with a history of right upper quadrant pain and eructation for six months. Cholecystectomy was performed in another hospital in November of that year and the patient returned in February 1957 with upper abdominal complaints. He was followed for three years, during which time there was recurrent upper abdominal pain, with

eventual development of biliary tract obstruction. Several barium-meal studies (Fig. 4) were performed between 1957 and 1960, but it was difficult to differentiate benign deformity due to adhesions from a malignant lesion. Operation in May 1960 revealed a mass in the head of the pancreas and dense adhesions, due to the previous cholecystectomy, from the omentum, colon, and stomach to the lower aspect of the right lobe of the liver.

CASE V: M. M., a 70-year-old male, was first seen in 1947 and followed until 1957. Eight years prior to examination a perforated gastric ulcer had been treated medically. Repeated barium-meal studies (Fig. 5) showed marked deformity of the antrum, a finding which was interpreted as due to fibrosis and perigastric adhesions related to the previous perforated ulcer.

CASE VI: T. K., a 77-year-old female, had been a regular patient in the Out-Patient Department since 1947. In 1927 she had undergone biliary tract surgery, followed by recurrent episodes of right upper abdominal pain, nausea, and vomiting. Repeated barium-meal studies in 1956, 1957, and 1959 (Fig. 6) showed a narrow antrum, normal mucosa, normal peristalsis; lack of complete distensibility in 1956 but distensibility in 1959. The condition was interpreted as benign, due to postoperative (post-cholecystectomy) adhesions.

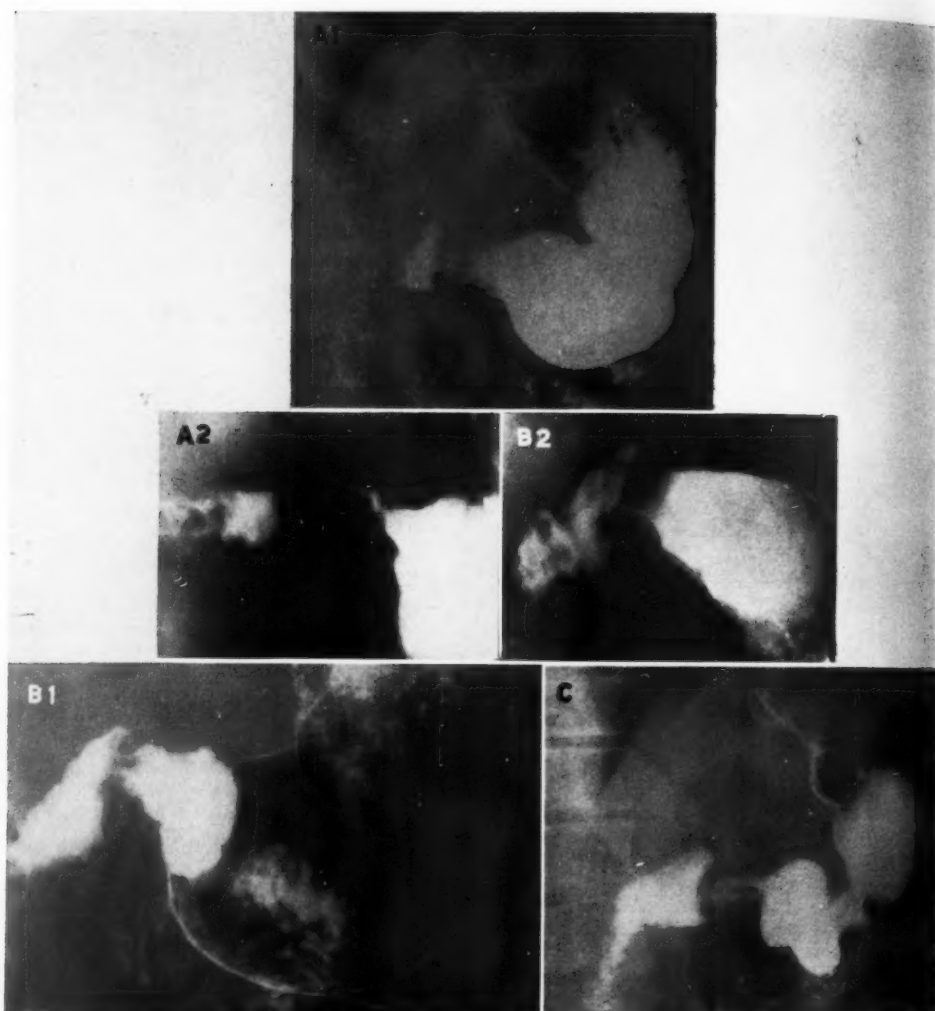


Fig. 4. Case IV: A-1 and A-2, Feb. 14, 1957. Prone oblique view and erect compression fluoroscopic film showing smooth antral deformity with normal distensibility, prominent folds, and poor peristalsis. B-1 and B-2, May 2, 1957. Fluoroscopic films showing good distensibility with carbonated beverage. C, April 22, 1958. Prone oblique view showing no change.

CASE VII: Y. D., a 60-year-old female, was admitted in 1956; a barium-meal examination (Fig. 7, A) prior to cholecystectomy showed normal findings. Symptoms of pyloric obstruction developed postoperatively. Antral and duodenal deformities with delayed emptying in the postoperative barium-meal study (Fig. 7, B) were interpreted as being due to postoperative adhesions.

CASE VIII: P. C., a 62-year-old female, was admitted in May 1958 because of right upper quadrant and epigastric pain of several months duration. Cholecystostomy had been performed thirty years

previously. A barium-meal study on May 6 (Fig. 8) showed narrowing of the antrum, but this was not interpreted as evidence of intrinsic gastric abnormality. At cholecystectomy on May 14, the entire right upper quadrant (including the antrum) of the abdomen was found to be fixed, due to adhesions from the previous cholecystostomy.

CASE IX: T. S., a 71-year-old female, was seen in 1958 with a two month history of obstructive jaundice. Operation revealed cholelithiasis, a mass in the head of the pancreas, lymph nodes suggestive of metastases (pathologic report: "reactive lymph



Fig. 4. Case IV: D1 and D2, June 1, 1959. Prone oblique and erect oblique views showing no significant change.

nodes"). The presumptive diagnosis was carcinoma of the head of the pancreas with lymph node metastases (not proved). Cholecystectomy and choledochoduodenostomy were performed. A postoperative barium-meal study (Fig. 9) showed antral deformity due to adhesions or extrinsic pressure of a mass rather than to intrinsic gastric carcinoma.



Fig. 4. Case IV: E, Feb. 23, 1960. Prone oblique view showing no progression. In May 1960, however, an operation revealed a mass in the pancreas and dense adhesions (due to previous cholecystectomy). This case demonstrates the difficulty in differentiating benign extrinsic adhesions from an extrinsic malignant lesion such as cancer of the pancreas.

CASE X: A. S., a 72-year-old male, gave a fifteen-year history of duodenal ulcer. He was admitted in 1959 with signs of acute perforation, which was confirmed at surgery and found to be at the pylorus. A barium-meal study two weeks postoperatively (Fig. 10) showed deformity of the prepyloric region due to operative repair.

STATISTICAL SURVEY TO RECORD INCIDENCE OF BENIGN PERIGASTRIC ADHESIONS

Since 1952, when our first patient was observed, the senior author (A. G.) has been especially interested in documenting examples of benign perigastric adhesions. From 1952 through 1959, 7 cases (Cases I-VI and X) were collected. Of these, 3 were postcholecystectomy, 3 followed perforation or repair of perforation of gastric or duodenal ulcer, and only 1 was due to a congenital band. This is in contrast to Jenkinson's 7 cases in 4 of which congenital bands were found.

The 3 cases in the present series due to postcholecystectomy adhesions raised the question as to the frequency of such find-

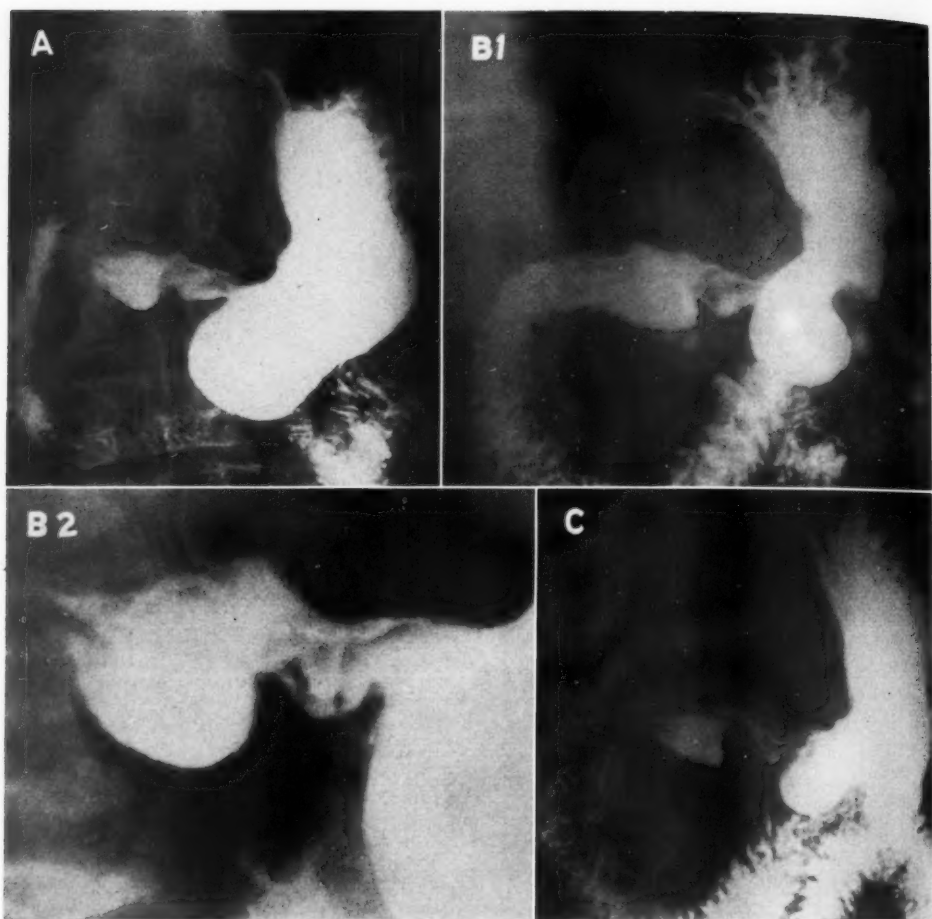


Fig. 5. Case V: A (1956), B (1953), and C (1948). Marked deformity of the antrum, with no progression over an eight-year period. *Diagnosis:* Perigastric adhesions related to previously perforated ulcer.

ings in a large group of patients with previous biliary tract surgery. Accordingly, the hospital records of all patients undergoing biliary tract surgery in the five-year period 1954-1958 were reviewed, as were all their gastrointestinal films, before and/or after surgery. Abnormalities of the antrum were specifically tabulated, together with the duodenal, esophageal, and extragastric lesions. In the abnormal cases, the operative and pathological reports were also reviewed. In this study, 3 additional cases were found, making the 10 cases reported in this paper.

1. *Results of Survey:* A total of 767 charts were reviewed. A barium-meal

examination had been performed in 128 cases; in 94 preoperatively only, in 7 both pre- and postoperatively, and in 27 postoperatively only. Altogether there were 34 postoperative studies, all undertaken because of symptoms. In 31 of the first group of 94 cases, abnormalities were found, including 22 duodenal bulb deformities and 6 antral deformities. Of the latter 6, 2 proved to be due to cancer of the pancreas; 1 was a gastric ulcer; 1 diagnosed radiologically as a prepyloric ulcer proved to be a duodenal ulcer with antral gastritis; in 1 case described as antral spasm and in 1 as atonic stomach the findings at operation were normal. Thus,

there was no instance of an antral deformity due to perigastric adhesions in this group of 94 studies prior to operation upon biliary tract.

Of the 7 patients with both pre- and postoperative x-ray studies there were 3 with normal and 4 with abnormal findings. Of the latter 4, 1 had an antral deformity (Case VII); 1 a deformed bulb; in 1 the finding was the result of a subtotal gastrectomy with obstruction in the early postoperative period; in 1 there was extrinsic pressure on the stomach from reticulum-cell sarcoma.

In the remaining 27 cases, with barium-meal studies carried out only postoperatively, there were 6 instances of deformed duodenal bulb and 4 of antral deformity. Three of the latter are described in detail—Cases VIII and IX of the group due to benign adhesions and Case XI due to cancer of the stomach (see p. 246). In the fourth case there was a prepyloric ulcer. There were 3 patients with other abnormalities: a mass due to pancreatitis (confirmed at operation), esophagitis, and delayed emptying.

Thus, in 5 of 34 patients with postoperative roentgen studies, antral deformities were found, 3 of which were due to adhesions. Of these, 1 was included in our original 7 cases. The incidence in the total group was less than 0.4 per cent (3 of 767). Of the 34 patients with postoperative roentgen examinations, 3 (9 per cent) had benign antral deformity, a significant figure. This is particularly noteworthy because of the ever increasing number of people in the general population undergoing biliary tract surgery, all of whom are candidates for perigastric adhesions. Cancer of the stomach or pancreas may also develop in these patients, and the fact that the adhesions may simulate cancer emphasizes the importance of documentation of the presence of adhesion-produced deformity and its differentiation by radiological criteria.

2. *Incidence of Post-Perforation or Post-Repair-of-Perforation Perigastric Adhesions:* Jenkinson *et al.* encountered no instance of

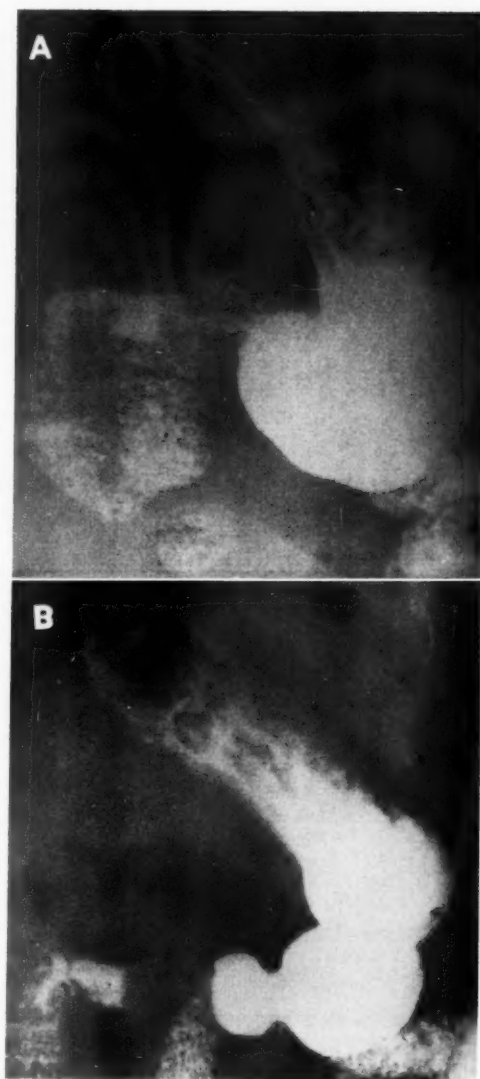


Fig. 6. Case VI: A (1956) and B (1959). Narrowing of the antrum, normal mucosa, normal peristalsis, incomplete distensibility. The findings were interpreted as being due to postoperative adhesions.

post-perforation or post-repair-of-perforation perigastric adhesions. In our series there are 3 cases in this category. In order to be certain that all such cases were documented, we reviewed all the charts of patients with perforated peptic ulcers for the years 1954 to 1958, the total number of which was not large. No additional examples were found.

DISCUSSION

1. *Nature of Congenital Band*

In only 1 of our cases (Case III) was a congenital band found, in contrast to 4 in Jenkinson's patients. The origin of such a band or adhesion becomes clear upon review of the embryological development and the adult anatomic relationships about the stomach. These subjects have been reviewed in detail by Jenkinson *et al.* in their report, with excellent illustrative drawings, and need not be repeated here.

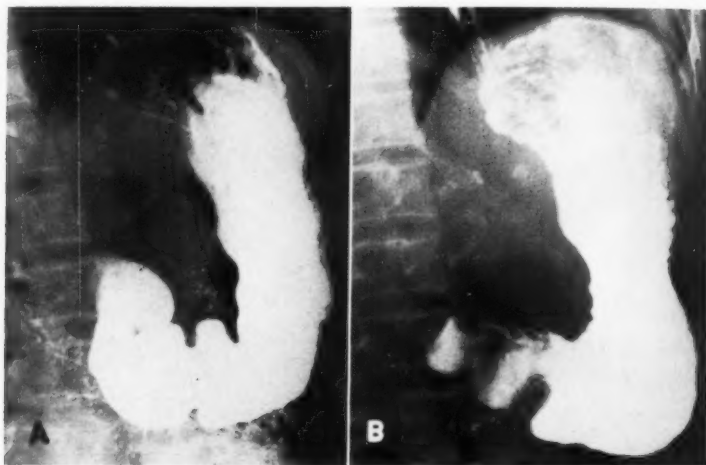


Fig. 7. Case VII: A. Prone oblique view—barium-meal examination prior to cholecystectomy—showing normal findings.
B. Barium-meal study one month after surgery, showing antral deformity with delayed emptying, interpreted as due to postoperative adhesions.

In our case exploration revealed an omental band lying over the antral and pyloric portions of the stomach from the greater omentum extending mesial and posterior to the gallbladder. Our case is similar to 2 of those of Jenkinson and his associates (Figs. 5 and 6 of their article; 8). An explanation of the development of symptoms so late in life is not simple. Jenkinson suggested that continued traction, low-grade inflammation, and changes in the habitus of the patient may be contributing factors.

2. *Significance of Postcholecystectomy Examinations*

In 3 (9 per cent) of the 34 cases studied by postcholecystectomy barium-meal roentgenography, antral deformity due to

perigastric adhesions was encountered, being noted as early as two weeks after surgery. This study suggests, therefore: (1) that a postoperative barium-meal examination is important in establishing a basis for subsequent change indicative of a superimposed malignant process; (2) that the postoperative barium-meal study may reveal an antral deformity early in the postoperative period; (3) that periodic roentgen examinations may be necessary to establish the correct diagnosis.

3. *Differential Diagnosis—Perigastric Adhesions vs. Gastric Cancer*

(a) *Normal Mucosa:* Because of the marked narrowing, demonstration of the mucosal pattern may be difficult. In none of the 10 cases was there a definitely abnormal pattern, although in Cases III and IV prominence of the mucosa was shown. The ulcer crater in Case II proved to be a pseudodiverticulum. A normal mucosal pattern, therefore, is significant in excluding a gastric cancer.

(b) *No Intramural Mass:* In none of the 10 cases was an intramural mass shown.

(c) *No Interval Change:* More than one examination was made in 5 of the 10 cases. In 4 of these there was no change. In Case IV change developed after three

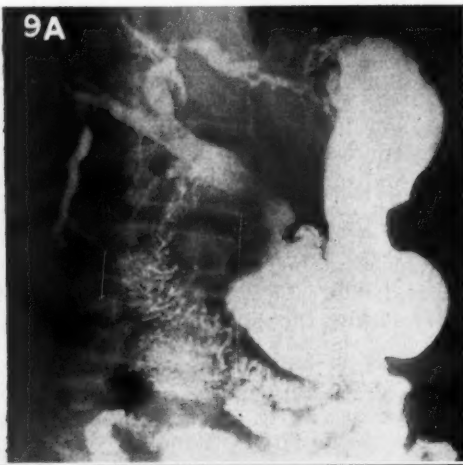


Fig. 8. Case VIII: Prone oblique view showing narrowing of the antrum. At surgery the antrum was found to be fixed, due to adhesions from a previous cholecystostomy.

Fig. 9. Case IX: Posterior anterior prone view (A) and fluoroscopic film (B) showing presence of choledochoduodenostomy performed three weeks previously. The antrum is narrowed due to adhesions and/or to extrinsic pressure of a pancreatic mass.

Fig. 10. Case X: Prone oblique view showing deformity of prepyloric region due to recent operative repair of acute perforation at pylorus.

years, due to an extrinsic lesion (carcinoma of the pancreas). Intrinsic gastric cancer is usually progressive.

(d) *No Infiltration:* The presence of infiltration is more difficult to determine, as it may be simulated by deformity due to anatomical distortion. In 6 of the 10 cases it was definitely noted that the deformed segment was not infiltrated.

(e) *Normal or Abnormal Peristalsis:* Peristalsis was normal in 5 of the 10 cases. In the other 5, it was sluggish, diminished, or absent in the antral segment. It can be hindered by dense perigastric adhesions as well as by intrinsic and/or extrinsic malignant invasion. Normal peristalsis, however, except at the point of adhesion, is a finding in favor of a benign lesion.

(f) *Localized Fixation, not Extensive:* Fixation, as well as narrowing of the antrum, was seen in 6 of the 10 patients. Localized rather than extensive fixation may point to a benign lesion.

Gastric cancer may develop in patients with previous cholecystectomy. The criteria for that diagnosis still hold—abnormal mucosal pattern, constant filling defects, intraluminal mass, infiltrative extension, and impairment of peristalsis. The following case illustrates these points:

CASE XI: S. P., a 70-year-old female, had undergone cholecystectomy two years previously. The roentgen diagnosis (Fig. 11) was cancer of the stomach, which was confirmed at operation. In addition, there were numerous dense fibrous adhesions of the liver, duodenum, omentum, and colon to each other and to the anterior peritoneum. The duodenum especially was densely adherent to the inferior surface of the liver, with foreshortening of the hepato-duodenal ligament accounting for some antral narrowing. Thus, despite the presence of dense postoperative adhesions, the diagnosis of gastric cancer could be made with some degree of certainty.

4. Differential Diagnosis—Perigastric Adhesions vs. Extragastric Malignant Lesions (Cancer of the Pancreas)

To differentiate perigastric adhesion from extragastric malignant lesions such as cancer of the pancreas is a dilemma not readily surmounted. All of the diagnostic criteria mentioned above may be unchanged even though a cancer of the pancreas has developed in the presence of benign perigastric adhesions, with a single exception—interval change. Even this may betray our diagnostic acumen, as in our Case IV. Here a cancer of the pancreas developed with no interval change over a period of almost three years in a patient with marked perigastric adhesions from a previous cholecystectomy. If an extragastric mass develops and can be so diagnosed on the roentgenogram, distinct from the distortion due to perigastric adhesions, then cancer of the pancreas can be suspected. We caution, therefore, that pancreatic cancer should not be overlooked in the presence of perigastric bands or adhesions.



Fig. 11. Case XI: Prone oblique view two years postcholecystectomy, showing antral narrowing with very large polypoid masses, extensive infiltration and impaired peristalsis. Preoperative diagnosis, carcinoma of the stomach, confirmed at operation. In addition, there were numerous dense fibrous adhesions accounting for some of the antral narrowing.

SUMMARY AND CONCLUSIONS

Ten cases of antral deformity due to perigastric adhesions or bands are presented: 6 due to previous biliary tract surgery, 3 to previous perforated peptic ulcer or operative repair of perforation, and 1 to a congenital band.

A survey of 767 postcholecystectomy patients suggests a significant incidence of adhesions following this operation.

Benign perigastric adhesions may be differentiated from carcinoma of the stomach, but it is more difficult to differentiate them from extrinsic malignant lesions adjacent to the stomach, especially carcinoma of the pancreas.

Because of the increasing number of persons who have biliary tract surgery, postoperative barium-meal studies are desirable as a baseline for detecting a subsequent change that may be evidence of gastric or pancreatic carcinoma.

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NOTE: The authors thank Dr. Seymour Zucker and Dr. Leon Ginzburg for permission to include Case III.

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SUMMARIO IN INTERLINGUA

Deformitate Antral, Causate per Perigastric Adhesiones o Bandas Simulante Carcinoma del Stomacho

Perigastric adhesiones e bandas que affice le antro pyloric pote resultar in un deformitate antral que simula—in le roentgenogramma—carcinoma del stomacho. A 8 previemente reportate casos de iste genere, 10 noves es addite: 6 causate per chirurgia del vias biliari, 3 per perforation o reparo de perforation in ulcere peptic, 1 per un banda congenite.

Esseva revistate le protocollos e—in tanto que disponibile—le roentgenogrammas gastrointestinal de 767 patientes subjicite a chirurgia del vias biliari. Inter 34 patientes in qui studios post-operatori esseva effectuate a causa de varie symptommas, deformitate antral esseva trovate in 5. In 3 le deformitate esseva causate per adhesiones.

Benigne adhesiones perigastric pote esser differentiate roentgenographicamente

ab carcinoma del stomacho, sed lor differentiation ab maligne lesiones extrinsec de sito adjacente al stomacho—specialmente carcinoma del pancreas—es plus difficile. Nulle del casos in le presente serie monstrava un definitemente anormal configuration mucosal. Nulle habeva un demonstration massa intramural. Absentia de infiltration e de alteration de intervallo, normalitate del peristalse, e fixation localisate plus tosto que extense etiam supporta le conclusion que le lesion es benigne.

A causa del crescente numero de subjectos in qui chirurgia del vias biliari es executate, studios post-operatori a repasto de barium es desirabile como base de referentia in le detection de subsequente alterationes indicante possiblemente carcinoma del stomacho o del pancreas.

Spontaneous Pneumoperitoneum in Appendicitis¹

BENJAMIN E. GREENBERG, M.D.

SPONTANEOUS pneumoperitoneum is infrequently encountered as a radiographic finding in association with a perforated appendix. This has led some authors to doubt that it occurs at all (11, 13). A review of the literature revealed a total of 10 cases reported by Vaughan and Singer (14), Guillemin (6), Kornblum (8), Spensley *et al.* (12), and Epstein (3). In most instances free intraperitoneal gas is a result of perforation of a peptic ulcer. The radiologist should, however, be aware of its occurrence in appendicitis with perforation in order not to mislead the surgeon.

The present report describes 2 cases and discusses the pathogenesis as well as the reasons for the low incidence of this complication.

CASE REPORTS

CASE I: J. W. W., a 59-year-old white male, gave a history of abdominal pain, at first periumbilical, then migrating to the left lower quadrant and gradually spreading across the entire lower abdomen. He was first hospitalized and treated with penicillin at a private hospital, where a diagnosis of ruptured peptic ulcer or perforated appendix was made. He appeared acutely ill; blood pressure 120/80. On admission to the VA Hospital, three days after onset, there was tenderness in all quadrants of the abdomen, most pronounced in the right lower quadrant. There was mild rebound tenderness. The bowel sounds were hypoactive. The white cell count was 16,900, with 95 per cent neutrophils; red cell count 4,550,000. Films of the abdomen (Fig. 1) revealed a small amount of free peritoneal air consistent with a perforated viscus.

Shortly after admission a diagnosis of ruptured viscus was made, the possibilities of ruptured sigmoid diverticulum, ruptured peptic ulcer, and ruptured appendix being considered. The patient was taken to surgery and a left McBurney's incision was made. On opening the peritoneum, a little air escaped. A large amount of moderately thick, yellowish-brown fluid was aspirated. The sigmoid colon was free of disease. The incision was closed and a right rectus incision was made. The stomach and duodenum appeared normal, but on exploration of the appendiceal area an abscess was found.



Fig. 1. Case I. Left lateral recumbent view. Arrow indicates gas between liver and diaphragm.

A necrotic appendix was identified and removed. Culture from the abdominal cavity revealed *E. coli*. Postoperatively a fecal fistula developed, which gradually improved spontaneously.

CASE II: B. B., a 56-year-old white male, gave a history of the onset of epigastric pain, which shifted to the right lower quadrant, about three weeks prior to admission. He was at first treated conservatively by a private physician. After about one week he noted a tender mass in the right lower abdomen. There had been frequent attacks of right lower quadrant pain during the preceding year, usually disappearing within twenty-four hours. His blood pressure was 110/60; pulse 90; temperature 100.2°. He appeared chronically ill.

Examination revealed a discrete tender mass above Poupart's ligament on the right, measuring 4 × 6 cm. No rebound tenderness was elicited. The red cell count was 4,300,000; hemoglobin 12.1 gm.; white cells 12,200, with 78 per cent neutrophils. Films of the abdomen (Fig. 2) showed a small amount of free air beneath the right diaphragm in the upright view and extrinsic mass pressure on the gas-filled cecum in the supine view. Moderate gaseous distention of the large bowel was present. The findings were considered consistent with a diagnosis of perforated hollow viscus with some paralytic ileus. The white cell count rose to 15,500 on the second day of hospitalization, the temperature rose to 101°, and the pulse to 100. A Levine tube was introduced into the stomach and attached to a Wangenstein suction apparatus.

¹ From the Radiology Service (Benjamin E. Greenberg, M.D., Chief) Veterans Administration Hospital, Memphis, Tenn. Accepted for publication in December 1960.

The patient was not passing gas by rectum and no peristaltic sounds could be heard.

On the third day of hospitalization the patient was taken to the operating room, where under spinal anesthesia a right McBurney incision was made. On exposure of the peritoneum, there exuded a greenish-yellow fluid, from which *E. coli* and *A. aerogenes* were grown. A large abscess was found about the cecum, containing some 350 c.c. of creamy pus. The appendix, which had sloughed, was found lying free in the abscess and contained a large fecalith at its base. The patient made a satisfactory recovery.



Fig. 2. Case II. Upright view. Arrow points to small amount of gas beneath diaphragm.

DISCUSSION

The incidence of pneumoperitoneum in perforated appendicitis is not known with certainty. During a ten-year period when 1,130 patients with appendicitis were admitted to our hospital, free intraperitoneal air was demonstrated only twice. This does not, however, indicate the true incidence, since in only about 200 of these cases was abdominal radiography done. In the remaining cases there appeared to be no indications for such studies. There were 98 cases of perforated appendix in the radiographed group. This would suggest an almost 2 per cent incidence of pneumoperitoneum in perforated appendi-



Fig. 3. Gas in a subhepatic normal appendix, in relation to a reversed cecum found in a combined oral cholecystographic and barium-enema examination that was otherwise negative.

citis. A lower incidence would be anticipated in a series in which radiography was performed routinely without selection. In fact, such a conclusion was reached by Frimann-Dahl (5), who in over 2,000 cases of acute appendicitis radiographed routinely failed to encounter a single example.

Only a small amount of air free in the peritoneal cavity is necessary for radiographic demonstration. Three cubic centimeters of air can be immediately detected beneath the diaphragm, and even 1 or 2 c.c. is recognizable, but only after prolonged upright positioning prior to radiography (7). The volume of air that could be contained in the lumen of the average normal appendix, if released into the peritoneal space, should be readily detected. The infrequent occurrence of such an event can be attributed to certain anatomical and pathological factors. First, the appendix does not generally contain air in its normal dependent position (10). If it lies in a subhepatic location, as in the presence of an undescended cecum or reversed cecum, it may contain air without being pathologic

(Fig. 3). Secondly, there is evidence that the lumen of a diseased appendix is reduced in a significant percentage of cases. In a study of 50,000 appendices, mostly surgically removed, Collins (2) found that the lumen was partly or completely obliterated in over one-third of the specimens. He also found that about one-fourth of the appendices were retrocecal in position. This third factor also lessens the possibility of free peritoneal air. It is thought that a retrocecal appendix is five times more prone to inflammation than one normally positioned (9). Perforations of retrocecal appendices are more readily sealed off.

Gas and a fluid level in a normally positioned appendix or gas alone, without evidence of fluid, may be a sign of suppuration (4). Gas may arise from growth activity of such gas-forming organisms as *E. coli*, *A. aerogenes*, *B. proteus*, and the *Klebsiella* species. Whether the gas in the pneumoperitoneum of a perforated appendix is of the same composition as normal intestinal gas or is the result of bacterial activity is of only academic interest to the radiologist. The gas in the normally positioned appendix is due to the occlusion of the lumen, with subsequent infection by gas-forming organisms. It is conceivable that sufficient gas may be present to be radiographically detectable if permitted to escape into the peritoneal cavity. In a case of retrocecal appendix in the present series the lumen was occluded and perforation occurred with gas retroperitoneally, appearing as linear streaks and bubbles in the psoas muscle region. There are two other possible methods for free peritoneal air to occur: from secondary perforation of an abscess containing gas and from peritonitis due to infection with gas-forming organisms. The latter possibility is only theoretical, since no proved case has to the writer's knowledge been reported.

SUMMARY

Two cases of spontaneous pneumoperitoneum associated with perforated appendicitis are added to 10 similar cases collected from the literature. The possibility of such a finding should be kept in mind to avoid misleading the surgeon. The infrequent occurrence is explained on anatomical and pathological grounds. Possible sources of the intraperitoneal air are the appendiceal lumen, perforation of a gas-containing abscess within or outside of the appendix, and (theoretically) peritonitis caused by gas-forming organisms.

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SUMMARIO IN INTERLINGUA

Pneumoperitoneo Spontanee in Appendicitis

Duo casos de spontanee pneumoperitoneo associate con perforation del appendice es addite al serie de 10 tal casos colligite ab le litteratura. Le possibilitate de un tal constatacion deberea esser memorate pro evitar malinformar le chirurgo. Le infrequentia del occurrentia de iste phenomeno es explicate a base de observationes anatomic e pathologic. Primo, le appendice in su normal position pendente non contine aere. Secundo, in le presentia de morbo, le lumine del appendice es reducite o obliterate in un considerabile

numero de casos. Finalmente, il ha essite constatate que approximativemente 25 procento del appendices es de position retrocecal. Durante que un appendice retrocecal debe esser reguardate como plus susceptible de inflammari se que un appendice in position normal, perforationes es recludite plus prestemente. Le fontes possibile de aere intraperitoneal es le lumine del appendice, perforation de un abscesso a contento gasose intra o extra le appendice, e (theoricamente) peritonitis causate per organismos que es generatores de gas.



Roentgen and Clinical Diagnosis of Glomus Jugulare Tumors

Four Cases and a New Radiographic Technic¹

SERVIO T. ERASO, M.D.²

GLOMUS JUGULARE tumors are rare. Few references to their occurrence are found in the American literature, greater attention having been paid to them in European countries. During the past few years we have encountered 4 cases of glomus jugulare tumor at the Ohio State University Health Center. These cases will be reported here, with special reference to the roentgenologic, angiographic, and clinical features. A special view designed by the author for facilitating their visualization will be described.

ANATOMY AND PATHOLOGICAL FINDINGS

The term glomus has been applied to small and sometimes minute neuromyo-vascular aggregations in the form of histologically recognizable bodies. These bodies are composed primarily of fine arterioles connecting directly with veins and rich in nerve supply. They are widely distributed throughout the body and are classified into two main groups. The first or central group includes the carotid, jugular, aortic, and coccygeal bodies. A glomus is also found in the ganglion nodosum of the vagus nerve. In the second or peripheral group are the small bodies in the skin, especially at the ends of the extremities, mainly in the fingers. The function of these bodies is still not completely understood, but they are generally regarded as chemoreceptor organs. The stimuli affecting the peripheral glomera are temperature, touch, and pressure. The stimuli which affect the central group, especially those located in the vessels, are increase in CO₂, diminution in oxygen tension, and alteration of pH in the blood. These two groups differ functionally from each other. Stimulation of the peripheral glomera causes only local effects, whereas stimulation of

those near the vessels produces systemic results.

Glomus tumors (glomangioma, non-chromaffin paraganglioma) represent hyperplasia of all the neuromyo-arterial elements of the normal glomus. They are found in many parts of the body, especially in the tips of the extremities, most commonly in the subungual region of the fingers. They also occur on the flexor surface of the arm, in the region of the knee, in the bones, and in the stomach. The central glomus tumors more frequently arise from the carotid and jugular bodies. Pain is the main symptom of the skin lesions, which are therefore known as painful subcutaneous tumors. In glomus tumors of the central group pain is not an outstanding clinical feature.

Glomus jugulare tumors arise from cell masses of exactly the same structure as the glomus caroticum. Such cell masses are partially located in the adventitia of the bulb of the jugular vein, near the tympanic branch (nerve of Jacobson) of the glossopharyngeal nerve, near the auricular branch (nerve of Arnold) of the vagus, and immediately below the bony floor of the middle ear.

The tumors may arise from the bulb of the jugular vein and may grow into the middle ear and from there into the external auditory meatus. They can destroy the petrous bone and extend into the cranial cavity. Others arise from glomus elements situated along the previously mentioned nerves and may extend to the geniculate ganglion and the descending portion of the facial nerve.

CLINICAL FINDINGS

Glomus jugulare tumors have been found most frequently in patients forty to sixty

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years old. They are rare before the age of twenty-five. They are more frequent in women than in men. The symptoms vary considerably with the location of the tumor and its extent. Growth is slow and the clinical picture is at first quite uniform. Usually the first symptom is impaired hearing and tinnitus on the side of the lesion. Pain is rare. The tumor sometimes fills the entire middle ear and can be seen projecting into the external auditory meatus as a polypoid mass with a

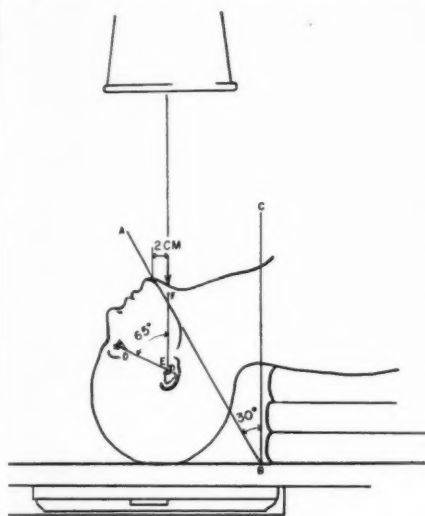


Fig. 1. The head is extended so that the lower border of the mandible is aligned with the line AB, which forms an angle of 30° with the perpendicular CB. The line DE from the external canthus to the tragus is 65° from the perpendicular FE passing through the tragus. (FE is not a prolongation of the central ray, although on the diagram it coincidentally appears to be so).

rich blood supply. Attempts at its removal may result in profuse hemorrhage. It causes paralysis of the 9th, 10th, and 11th nerves, which are involved in the jugular foramen and of the 7th and 8th nerves by destruction of the petrous bone. In some patients there is paralysis of the 12th nerve due to extension of the lesion to the hypoglossal canal.

ROENTGENOGRAPHIC FINDINGS

Glomus jugulare tumors are difficult to demonstrate roentgenographically, since



Fig. 2. Position of the patient with pillows under the back and shoulders. The movable radius bar of the protractor is 30° from the perpendicular, and the lower border of the body of the mandible is aligned with it. The central ray is 2 cm. below the symphysis of the mandible. (These positioning factors apply to dentulous patients.)

most of them arise from the bulb of the jugular vein, which lies in the jugular foramen. They are best seen on a special view devised by the author. The radiologic findings are enlargement of the jugular foramen on the side of the lesion associated with destruction of the petrous bone and also of the lateral part of the occipital bone. Angiographically the tumor stain resembles that of meningioma.

Technic for Demonstration of Jugular Foramina: A well established roentgenographic technic for demonstration of the jugular foramina has not previously been described. The author's view shows the jugular foramina in good detail. The following positioning and factors are used:

If the patient has teeth in both jaws

1. Supine position.



Fig. 3. Routine basal view showing the BB shot in the left jugular foramen, which is obscured by the superimposed petrous bone.

2. Shoulders and trunk elevated by a mattress or pillows sufficiently to let the vertex rest on the table surface (Fig. 2).
3. Inferior border of the body of the mandible adjusted along a line (AB) 30° from the vertical (BC) to the table (Fig. 1). An Angligner device may be used (Fig. 2).
4. The symphysis of the mandible in the midline.
5. The central ray passes through a point 2 cm. below the symphysis of the mandible and is perpendicular to the film (Figs. 1 and 2).
6. With Par Speed screens, 125 mas and 74 kv are used for average skulls. A target-film distance of 40 inches and a 10×12 -inch film with appropriate cone are employed.

If the patient is edentulous

An angle of 65° should be used; this angle is formed by a line (FE) perpendicular to the table, passing through the tragus, and a line (DE) connecting the external

canthus to the tragus (Fig. 1), all other factors remaining the same.

On the routine basal view of the skull the jugular foramen is obliterated by the petrous bone, as seen in Figure 3. In this picture a BB shot was placed in the center of the jugular foramen on the left. On the Waters view, the foramen is obliterated by the body of the mandible. The new position demonstrates with good detail both jugular foramina, as seen in Figure 4, with the BB shot in the middle portion of the left foramen. It is also seen in Figure 5, showing the typical bean-shaped foramina.

CASE REPORTS

CASE I: A 53-year-old white female entered University Hospital on Jan. 23, 1956, complaining of left-sided deafness and facial paralysis. She gave a history of "boils" in the left ear when she was in her twenties. The deafness had been progressive, until at the time of admission it was almost total. Two months prior to admission the patient noted the onset of drooling from the left side of the mouth, difficulty in closing the left eye, progressive left-sided paralysis of the face, and a change in her voice. The left external auditory canal contained grayish tumor with dilated capillaries on the surface. Neurologic examination showed left peripheral facial paralysis, air-conduction deafness but normal bone conduction on the left, and normal hearing on the right. The uvula was deviated to the right, and there was paralysis of the left vocal cord, weakness of the left sternocleidomastoid muscle, and paralysis of the 7th, 8th, 9th, 10th, and 11th cranial nerves on the left. X-ray films of the skull demonstrated destruction of the jugular foramen and adjacent parts of the petrous and occipital bones on the left (Fig. 6). Biopsy showed glomus tumor.

CASE II: A 58-year-old colored woman entered the hospital on Aug. 12, 1956, because of hoarseness. For the past seven years she had had a dull aching and pulling sensation in the sternocleidomastoid muscle and hoarseness due to paralysis of the left vocal cord. On biopsy of the vocal cord a polyp was found. There was no difficulty in eating or swallowing. Hearing ability on the left was approximately one-half of normal. Some loss of sensation in the pharynx was noted. The left trapezius muscle was weaker than the right. The tongue deviated to the left, with atrophy of the left side. A bruit was heard at the base of the mastoid on the left. Films of the skull showed enlargement of the jugular foramen on the left.

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Fig. 5.

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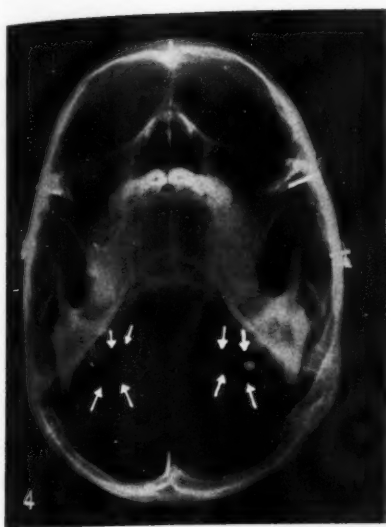


Fig. 4. The jugular foramen is well seen in this view, obtained with the position and factors illustrated in Figs. 1 and 2. The BB shot is located in the left jugular foramen.

Fig. 5. Both jugular foramina are well seen in this normal patient.

CASE III: A 67-year-old white woman entered the hospital on April 6, 1959, for evaluation of persistent right-sided deafness. She admitted having had dysphasia and dysphagia for ten years. During the year previous to admission, she had suffered bilateral mandibular aching pain, with a mass under the right ear. A peripheral type 7th nerve palsy was present on the right side. Other findings included: chronic otitis media on the right, slight enlargement of the left pupil as compared to the right, and complete paralysis of the 7th to the 12th cranial nerves.

X-ray films of the skull showed destruction and erosion of the petrous pyramid and lateral part of the occipital bone. On fluoroscopy of the pharynx, the barium was delayed in the vallecula, giving a positive vallecular sign. A vertebral arteriogram demonstrated homogeneous opacification of the tumor adjacent to the petrous pyramid of the right side, resembling a meningioma (Fig. 7). A middle ear biopsy showed a glomus tumor.

CASE IV: A 56-year-old white woman was admitted on April 12, 1959, with a history of itching about the mouth for twenty years, draining from the right ear associated with occasional pain, dysphagia, vertigo, loss of hearing on the right, and right facial paralysis. Three years earlier a "growth" had been removed from the external auditory canal on the right. According to the patient this had improved her hearing.

On examination, a grayish-red mass was found in the right external auditory canal. There was weakness of the right trapezius muscle. X-ray films revealed erosion of an enlarged right jugular



Fig. 6. Case 1: The right jugular foramen is sharply outlined and of normal size. The left jugular foramen is enlarged, and the adjacent portions of the petrous and occipital bones are destroyed.

foramen and of the adjacent bones (Fig. 8). A specimen obtained on partial excision showed glomus tumor.

SUMMARY

Four cases of glomus jugulare tumors are reported. The roentgenograms, including one arteriogram, are presented and



Fig. 7. Case III: A right vertebral arteriogram showed a homogeneous tumor stain resembling a meningioma.

the literature is reviewed. All four patients were adult females. The most outstanding symptoms were deafness and peripheral facial nerve paralysis on the side of the lesion. Roentgenographically the tumors are best demonstrated by a special jugular foramen view devised by the author.

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SUMMARIO IN INTERLINGUA

Diagnose Roentgenologic e Clinic de Tumores de Glomus Jugular, con Reportos de Quatro Casos e un Nove Technica Radiographic

Tumores de glomus jugular es micre aggregationes neuromyovascular que prende lor origine in massas cellular locate partialmente in le adventitia del bulba del vena jugular proxime al branca tympanic del nervo glossopharyngee, proxime al branca auricular del vago, e immediateamente infra le fundo ossee del aure medie.

Le prominente symptomatas es surditate e

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Fig. 8. Case IV: The left jugular foramen is sharply outlined and of normal size and configuration. On the right the jugular foramen is enlarged, with considerable destruction of the adjacent petrous bone and a lesser degree of destruction of the occipital bone.

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paralyse de nervo peripheric al latere del lesion. Le constatationes radiologic es allargamento del foramine jugular a iste latere, associate con destruction del osso petrose e etiam del parte lateral del osso occipital. Es describe un technica, elaborate per le autor, pro demonstrar le foramines jugular. Es reportate quatro casos.

Preoperative Irradiation in Rectal Carcinoma¹

ROBERT H. LEAMING, M.D., MAUS W. STEARNS, M.D., and MICHAEL R. DEDDISH, M.D.

THE USE of preoperative irradiation has been controversial for some time. It was formerly discouraged because of operative delay, added expense, and, when large dosage was used, occasional technical difficulties at the time of surgery secondary to radiation damage to normal tissue.

In general, most adenocarcinomas represent neoplasms refractory to external irradiation with exceptions based on anaplasia and site. Most of us agree, for example, that in the treatment of endometrial adenocarcinoma the preoperative irradiation may bring about unquestionable improvement in the end-results of surgery.

The late George Binkley was one of the pioneers in attempting to improve surgical results by radium and x-ray therapy. Through his foresight and that of his followers, irradiation has been employed as a preoperative agent at Memorial Center for the last twenty years. Prior to 1917, surgery was the only method used for the treatment of rectal carcinoma. From the late 1920's through the 1930's, a considerable effort was made to treat this neoplasm solely by various forms of ionizing radiation. Interstitial radium and radon, radium applicators and packs, and high-voltage roentgen rays were used extensively enough to prove that, except in a small number of patients, these modalities could not at that time be considered curative. By the end of the 1930's irradiation was no longer used for patients considered amenable to cure. Binkley concluded, however, that for inoperable, recurrent, or metastasizing cancer of the large bowel roentgen therapy was the most generally useful agent for palliation. He recognized, moreover, the importance of treating the primary tumor and surrounding lymphatics by the initial use of external irradiation in the form of a

"pelvic cycle or bath," *i.e.*, x-ray treatment through multiple ports.

MATERIAL AND DATA

To evaluate possible effects of preoperative irradiation in the management of rectal cancer, we have reviewed the charts of 1,786 patients with histologically proved adenocarcinoma of the rectum or rectosigmoid, not previously subjected to surgery, seen by members of the rectal and colon service of Memorial Center during the years 1939 to 1951. Of this series, 510 were not subjected to celiotomy: some of these were seen in consultation only, some refused preferred treatment or failed to complete treatment, and others were considered inoperable. One thousand, two hundred and seventy-six patients (72 per cent) submitted to exploratory procedures. Of these, 971 (77 per cent) had resections of the involved segment of bowel, an overall resectability rate of 54 per cent.

The patients subjected to celiotomy were divided into two groups, those who received preoperative irradiation and those who did not. The preoperative cycle was delivered with a 200-kv machine with h.v.l. of 1.0 mm. Cu. The patients were routinely treated by a six-field technic, with two anterior, two posterior, and two lateral pelvic ports measuring 14×11 cm., at a target-skin distance of 70 cm. If the primary lesion was located within 8 cm. of the anal verge, a perineal cone 10 cm. in diameter was added, with treatment at 250 kv, h.v.l. 2.0 mm. Cu, and target-skin distance 50 cm. An exposure dose of 900 r (air) was delivered to the lateral and posterior ports and 450 r (air) to the anterior ports. The fields were routinely oriented in such a manner as to cover the primary lesion and regional lymphatics.

¹ Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

Diagram 1 illustrates the type of distribution that might be expected with the six-field technic. With such a treatment plan, the maximum tissue dose is 1,200 r and the minimum tissue dose is 800 r. When the perineal cone is used with the six-field technic, an additional 450 r is delivered to the primary tumor.

The operative mortality is presented in Table I. The overall figure was 2.8 per cent, while for those subjected to resection it was 2.3 per cent. There was no significant difference between those who had received previous roentgen therapy and those who had not.

The data related to survival are in-

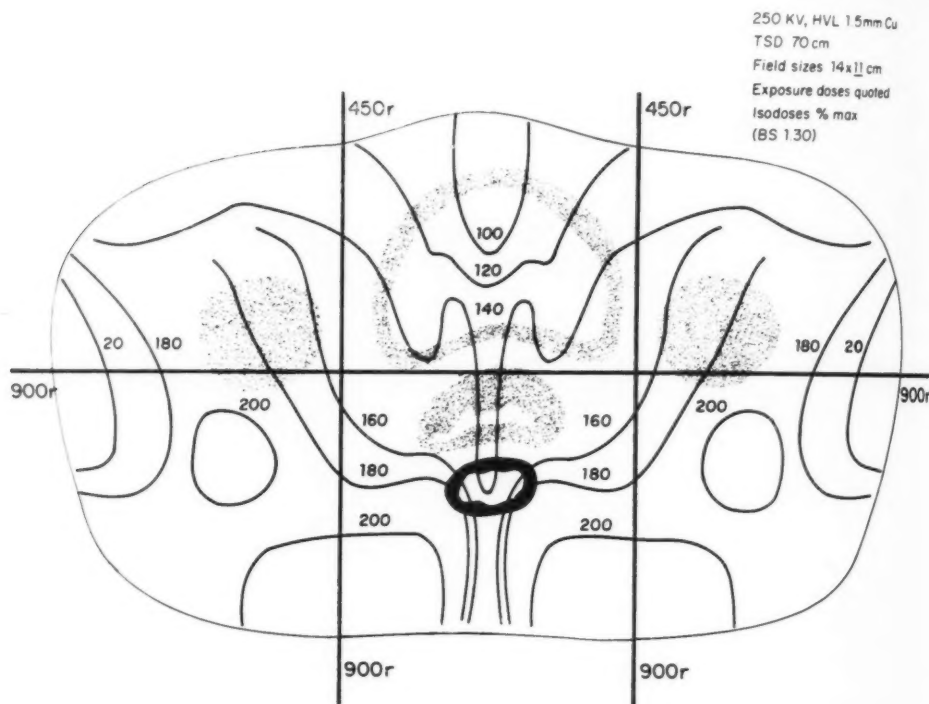


Diagram 1. Dose distribution to be expected with six-field technic.

The daily dose rate was somewhat higher than usual, that is, 450 r in air to a single pelvic port. In the usual case, this was delivered in a period of ten to twelve treatment days or an overall time of two weeks. With this dosage a mild erythema is produced, evidenced over a prolonged period by a slight tanning of the skin. This in no way interferes with subsequent surgery or healing. There are no untoward effects secondary to the irradiation during the preoperative period and actually many patients are reluctant to follow through with resection because their bowel symptoms are alleviated.

TABLE I: OPERATIVE MORTALITY

	Total Patients	Postoperative Deaths
Operated upon	1276	37 (2.8%)
No x-irradiation	549	14 (2.6%)
With x-irradiation	727	23 (3.0%)
Resected	971	22 (2.3%)
No x-irradiation	473	11 (2.3%)
With x-irradiation	498	11 (2.2%)

corporated in Table II. There were 505 patients who survived five or more years, an overall survival rate of 28.5 per cent. For those subjected to operation the five-year survival rate was 37.4 per cent and

TABLE II: FIVE-YEAR SURVIVAL

	Total Patients	Five-Year Survivals
Total series	1786	505 (28.5%)
Operated upon	1276	479 (37.4%)
No x-irradiation	549	225 (41.0%)
With x-irradiation	727	254 (35.0%)
Resected	971	479 (49.0%)
No x-irradiation	473	225 (47.5%)
With x-irradiation	498	254 (51.0%)

for those having some type of resection, 49 per cent. It should be emphasized that these are overall figures; cases were considered as failures if the patients were lost to follow-up or died of other cause, without evidence of cancer, in less than five years, as well as if there were distant metastasis at the time of treatment.

The patients operated upon were divided on the basis of preoperative irradiation. The overall five-year survival rate was 41 per cent for those who did not receive treatment preoperatively and 35 per cent for those who did. When the patients with resection of the primary neoplasm were similarly grouped, the five-year survival rate in those without preliminary x-ray therapy was 47.5 per cent against 51 per cent for those with preoperative irradiation. This figure includes patients with palliative resection in the presence of distant metastasis.

In an effort to determine whether preoperative roentgen therapy might be of value in particular types of patients or tumors, the patients with resections were separated on the basis of age, sex, grade of tumor, and Dukes' classification of the

TABLE III: SURVIVAL AND AGE, SEX, AND GRADE OF TUMOR

	No. of Patients	No. of Five-Year Survivors
<i>Age</i>		
Under 40		
No x-irradiation	28	12 (43%)
With x-irradiation	36	25 (70%)
40 to 49		
No x-irradiation	75	46 (61%)
With x-irradiation	99	54 (55%)
50 to 59		
No x-irradiation	133	69 (52%)
With x-irradiation	152	73 (48%)
60 to 69		
No x-irradiation	138	68 (49%)
With x-irradiation	151	81 (54%)
Over 70		
No x-irradiation	42	14 (33%)
With x-irradiation	38	14 (37%)
<i>Sex</i>		
Males		
No x-irradiation	202	97 (48%)
With x-irradiation	290	152 (52%)
Females		
No x-irradiation	169	90 (53%)
With x-irradiation	188	105 (56%)
<i>Tumor Grade (Dukes)</i>		
I		
No x-irradiation	7	5 (71%)
With x-irradiation	8	6 (75%)
II		
No x-irradiation	232	132 (57%)
With x-irradiation	238	146 (61%)
III		
No x-irradiation	101	43 (43%)
With x-irradiation	178	84 (47%)
IV		
No x-irradiation	6	1 (17%)
With x-irradiation	6	2 (33%)

resected specimen. These data are contained in Tables III and IV.

It may be seen that preoperative irradiation influenced survival favorably only in those patients with lymph node metastases in the resected specimen (C in Dukes' classification). The survival rate in those without x-ray treatment was 23

TABLE IV: SURVIVAL AND DUKES' CLASSIFICATION

Dukes' Classification	No. of Patients	Incidence in Series (%)	Liver Metastasis	Indeterminate	Five-Year Survivors	Overall Five-Year Survival (%)	Determinate Five-Year Survival (%)
A							
No x-irradiation	96	21	0	8	69	72	79
With x-irradiation	103	23	2	15	75	73	85
B							
No x-irradiation	145	33	0	12	92	63	70
With x-irradiation	161	35	2	12	104	64	70
C							
No x-irradiation	201	46	19	10	46	23	25
With x-irradiation	195	43	13	14	72	37	43

TABLE V: FIVE-YEAR RESULTS ACCORDING TO DOSE

	Total No. of Determinate Cases	Five-Year Survivors
Dukes' A		
One cycle or less	11	8 (73%)
Two cycles or more	74	65 (88%)
Dukes' B		
One cycle or less	22	13 (60%)
Two cycles or more	125	92 (74%)
Dukes' C		
One cycle or less	33	14 (42%)
Two cycles or more	143	60 (42%)

per cent; in those who had received such irradiation, 37 per cent.

Table IV also indicates that the relative distribution of Dukes' A, B, and C lesions was similar in both series. The indeterminates include those who died post-operatively or of other causes or were lost to follow-up without evidence of recurrent or metastatic cancer in less than five years. The determinate five-year survival figures exclude cases operated upon for palliation and the indeterminate patients.

Results of preoperative irradiation according to Dukes' classification and average dose are compared in Table V. Successful five-year results with one pelvic cycle or less are compared with those following two or more cycles. This grouping was used because of the paucity of patients receiving less than one or more than two pelvic cycles. About 85 per cent of those patients who had an adequate cancer resection had been treated by the six- or seven-port technic described earlier. No valid conclusions of any statistical significance can be drawn, but there is an interesting trend toward a more successful five-year survival rate in those patients who had two or more cycles.

The incidence of gross metastasis to the liver as related to preoperative irradiation is reviewed in Table VI. The overall incidence in those with and without preoperative irradiation was 18.5 per cent and 11.2 per cent respectively. An effort was made to ascertain whether this higher incidence of gross liver metastasis was a reflection of undue delay introduced by the administration of preoperative irradiation. Thus, the patients were grouped and com-

TABLE VI: LIVER METASTASIS

	No. Explored	Metastasis Present
No x-irradiation	540	62 (11.2%)
With x-irradiation	727	138 (18.5%)
<i>Time Interval to Surgery</i>		
Under 1 month		
No x-irradiation	476	57 (12%)
With x-irradiation	184	25 (14%)
1 to 3 months		
No x-irradiation	42	4 (10%)
With x-irradiation	466	89 (19%)
3 to 6 months		
No x-irradiation	11	1 (10%)
With x-irradiation	72	19 (27%)
Over 6 months		
No x-irradiation	13	2 (15%)
With x-irradiation	39	18 (46%)

pared according to time intervals which elapsed between the dates of initial x-ray therapy and surgery for those who received preoperative irradiation, and between the dates of initial visit and surgery for the others.

DISCUSSION

We believe there is a definite rationale for the use of preoperative irradiation as evidenced by the following:

1. There is less likelihood of radiation-damaged tumor cells being disseminated or implanted at subsequent surgery.
2. Tissue planes are not disturbed by a dose of the magnitude employed.
3. Resection has been facilitated by shrinkage of large bulky lesions.
4. There is an ultimate decreased vascularity of the tumor following irradiation.

The first striking difference shown in this review is in the resectability rates of those who did not have preoperative irradiation (86 per cent) and those who did (69 per cent). That is, the patients who received preoperative roentgen therapy appeared to have a significantly lower resectability rate. In evaluating the significance of this disparity, one must consider the fact that all patients seen, regardless of the state of operability, are included: the borderline operable who were irradiated before exploration and a large number who were deemed inoperable and treated by irradiation with subsequent colostomy merely to relieve ob-

struction. Because of these considerations, we believe the lower resectability rate in the patients with preoperative irradiation cannot be ascribed solely to the use of this preliminary measure.

Under these conditions, it is our opinion that it is more meaningful to determine the difference in survival attributable to x-ray therapy by comparing patients who had resections instead of all patients operated upon. Thus, in the entire operative group the overall survival rate was 41 per cent for those who did not have preoperative irradiation against 35 per cent for those who did. If only the resected group is considered, the survival rate was 47 per cent for those without irradiation against 51 per cent for those irradiated. These figures would appear to indicate that the chance of long survival was not adversely affected by preoperative irradiation.

That preoperative irradiation actually benefited certain patients is indicated in Table IV, in which the series is divided according to Dukes' classification. This shows that, although preoperative irradiation did not influence the survival rate in patients without lymph node involvement, it did improve the survival in those with node metastases from 23 to 37 per cent. This improved overall survival rate of 14 per cent in a series of this size is highly significant. Thus, even though preoperative irradiation had no appreciable effect on lesions treated satisfactorily by standard surgical methods, it did substantially improve the salvage in the group currently having the poorest surgical outlook. The ten-year survival rate for the Dukes' C patients was 27 per cent for those who had received preoperative irradiation and 10 per cent for those who had not.

Another interesting finding in this review was the significantly higher incidence of liver metastases in patients with preoperative x-ray therapy—18.5 per cent compared with 11.2 per cent in those without. The explanation for this may lie, at least in part, in the fact that most of those patients considered inoperable or borderline operable had preoperative x-irradiation.

That this may not be the entire explanation is implied in the fact indicated in Table VI, namely, that with longer time intervals before surgery, the incidence of liver metastasis appears to increase more rapidly among those treated with x-ray. Differences are statistically significant when the delay was over six months. This observation, taken in conjunction with the apparent progressive increase over the shorter intervals, suggests that preoperative irradiation to a rectal cancer may give rise to a greater incidence of liver metastasis when surgery is delayed. From the data available, it would seem that, if an operation is performed within a reasonable time (one month) after roentgenotherapy, no increased risk of liver metastasis exists. It can be argued, however, that this is an evaluation of only gross liver metastasis palpable at the time of operation and that those without preoperative irradiation would be expected to have a smaller incidence of liver metastasis at surgery even after six months because here the cases are not likely to be inoperable or borderline operable.

In evaluating the effect of dose with Dukes' classification and five-year survival, it is to be borne in mind that 85 per cent of those patients with a cancer resection received treatment through six or seven ports, with a minimum dose of 1,200 r and a maximum of 1,600 r. We make no pretense that the lymphatics of those Dukes' C lesions were sterilized with a tissue dose of this magnitude, but it is quite likely that bulky, apparently inoperable lesions were made operable by relief of an associated inflammatory process. Regardless of the mechanism involved, there was a decided beneficial result in the Dukes' C cases with preoperative irradiation. It is our considered opinion that, until better criteria have been established for selecting patients for preoperative irradiation (or an equally effective adjunct to surgery is developed), patients with primary adenocarcinoma of the rectum should undergo a course of irradiation preoperatively. This belief is

TABLE VII: COMPARISON OF LARGE SERIES OF PATIENTS WITH RECTAL CARCINOMA TREATED BY SURGERY ALONE WITH THE PRESENT SERIES

Method	Author	No. of Cases	Five-Year Survival— (%)		
			Dukes' A	Dukes' B	Dukes' C
Surgery	Gabriel	142	90	65	20
Surgery	Grinnell	124	100	43	23
Surgery	Memorial	442	72	63	23
X-rays and surgery	Memorial	459	73	64	37

based on the improved survival rate in the patients currently having the worst prognosis, those with metastasis to mesenteric lymph nodes.

A comparison of large series of patients with rectal carcinoma treated by surgery alone with the present series illustrates the effective increase in five-year survivals in Dukes' C lesions (Table VII).

Recently we have increased the size of the pelvic ports and are using supervoltage for more adequate delivery of a homogeneous dose to the pelvic area and levels of node metastases. We are exploring the possible advantages of increasing the depth dose in the patients treated preoperatively, since with the conventional preoperative cycle this is only about 1,500 r.

At present our program calls for randomization of treatment of all rectal carcinomas. Patients whose birth dates fall on odd days receive preoperative irradiation; the others are operated upon directly.

There appears to be no doubt that refinements in technic will lead to better results. Here we have sought merely to emphasize the importance of preoperative irradiation in the ultimate improvement of results when it is followed in four weeks by an adequate cancer operation.

SUMMARY

1. Statistics on 1,786 patients with primary adenocarcinoma of the rectum or rectosigmoid seen at Memorial Center between 1939 and 1951 are reviewed. Of this number, 1,276 were subjected to celiotomy, 727 with preoperative x-ray therapy and 549 without.

2. In the first of these groups the resectability rate was 69 per cent, compared with 86 per cent in the second group. Probable explanations for this difference are given.

3. The overall five-year survival rate in the entire series was 28.5 per cent. The survival rate for patients subjected to celiotomy was 37.4 per cent; for those in whom a resection was performed it was 49 per cent. For those patients subjected to celiotomy when preoperative irradiation had not been given, the five-year survival rate was 41 per cent; with roentgen therapy it was 35 per cent.

4. When resection was accomplished, the five-year survival rate was 47.5 per cent if no irradiation had been given preoperatively, and 51 per cent if it had.

5. Age, sex, and grade of tumor did not appear to bear any relation to possible selection of patients for preoperative x-ray therapy.

6. Preoperative x-ray therapy did not seem to influence the survival rate in patients free of lymph node metastasis but definitely benefited those demonstrating lymphatic spread. With metastasis, the five-year survival rate in those not subjected to preoperative irradiation was 23 per cent; it was 37 per cent in those who were thus irradiated.

7. We believe that all patients who have had the benefit of preoperative irradiation should be operated upon within one month to exclude any apparent association of increased liver metastasis with preoperative delay. This association is statistically significant with lapses of six or more months between irradiation and definitive surgery.

8. It would seem that preoperative radiotherapy has a greater value than as a mere anti-inflammatory agent. In our series it has resulted in a significant increase in five-year results in Dukes' C lesions. To our knowledge this is the first acceptable clinical evidence of the value of a tissue dose of 1,500 r preoperatively in a primary adenocarcinoma.

All of the cases were treated by 200- to

250-kv machines with h.v.l. of 1.5 to 2.0 mm. Cu, a technic that can be reproduced in offices or hospitals without access to supervoltage.

9. An appeal is made for use of preoperative irradiation in rectal carcinoma. Since 80 per cent of these patients are said (Williams) to have some form of treatment other than surgery, why not deliver irradiation under the most ideal conditions, *i.e.*, prior to operation.

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SUMMARIO IN INTERLINGUA

Irradiation Pre-Operatori in Carcinoma Rectal

Inter le 1.786 patientes con adenocarcinoma primari del recto o rectosigmoide vidite al Centro Memorial inter 1939 e 1951, 1.276 esseva subicite a celiotomia: 727 de illes recipeva therapia a radios X ante le operation, 549 non. In le prime gruppo le incidentia de resectionabilitate esseva 69 pro cento, in le secunde 86 pro cento. Explicationes probabile pro iste differentia es presentate.

Le superviventia quinquenne pro le serie total esseva 28,5 pro cento; in le celiotomisatos illo esseva 37,4 pro cento; in le resectionatos illo esseva 49 pro cento. Inter le patientes subicite a celiotomia le superviventia quinquenne amontava a 41 pro cento in le absentia de irradiation pre-operatori. Illo esseva 35 pro cento con irradiation preliminar. In le gruppo resectionate, le superviventia quinquenne esseva 47,5 pro cento in le absentia de irradiation pre-operatori e 51 pro cento con irradiation preliminar.

Irradiation pre-operatori non pareva influentiar le superviventia in patientes libere de metastases in nodos lymphatic; illo definitemente beneficiava patientes con extension lymphatic. In le presentia de metastases, le superviventia quinquenne in patientes non irradiate ante le operation amontava a 23 pro cento, in comparison con 37 pro cento in patientes qui esseva irradiate in ille maniera.

Le autores opina que omne patiente qui ha recipite le beneficio de irradiation pre-operatori debe esser operate intra un mense pro excluder le apparente association inter augmento de metastase hepatic e retardo pre-operatori. Radiotherapia pre-operatori es de valor in ultra de su effecto anti-inflammatori: illo ha resultate in un augmento significative del successos quinquenne in le presentia de metastases de nodo lymphatic (lesion C de Dukes).

Sin dubita, raffinamentos de technica va meliorar le resultados.

The Effect of Radiation on Mammalian Nerve¹

MARY C. ARNOLD, Ph.D., FRANK HARRISON, Ph.D., M.D., and FREDERICK J. BONTE, M.D.

EFFECTS OF radiation on the nervous system may be conveniently grouped in two major categories: structural and functional. Until recent years, the literature has been almost devoid of reports of morphological alterations following irradiation of the nervous system. In 1936, a summarization of articles in this area required less than a single page in a two-volume work on the biological effects of radiation (1). Since that time, new modes of approach have necessitated a reassessment of the view that the nervous system is highly radioresistant. Electron microscopy has contributed new information. In 1942, Lawrence Reynolds (2) showed with the polarized light method of observation that myelin derangement followed administration of a single dose of 1,200 r of 550-kv x-rays to the brain. In the following year, however, on the basis of older investigative methods, Warren (3) reported that therapeutic doses of radiation had no appreciable effect on nerve tissue. More recently, necrotic oligodendroglial cells and occasional necrotic neurons in the pyramidal lobe and olfactory brain of experimental animals have been found by Hicks and Montgomery (4) after 1,200 r of 200-kv x-rays in a single exposure.

Postmortem examination of nervous tissue from persons who had previously been given therapeutic doses of x-rays has revealed degenerative changes. The morphological derangements were in areas which were not involved in the disease process under treatment, but were incidentally included in the treatment fields. More will be said about these clinical cases later in this paper.

Reports of functional alterations have been far more plentiful. Some of the

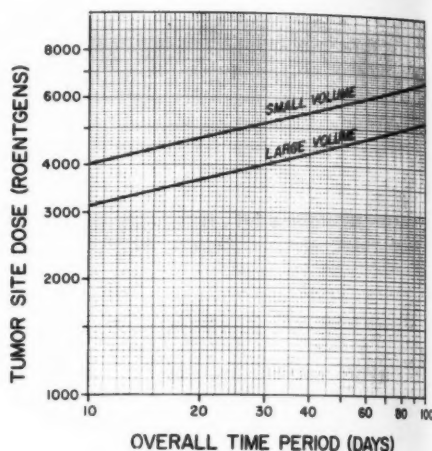


Fig. 1. Relationship between total dose and overall treatment period. After Boden in Murphy (10).

recent Russian work is of interest in that it cites measurable changes of nervous activity with doses as low as 0.05 r. Tsy-pin and Grigoryev (5), for example, describe changes in brain bioelectrical activity in the first ten seconds following exposure to doses of 0.05 to 1.3 r. Behavioral changes have also been found to occur at low dosage levels. Kudritsky (6) claims that conditioned reflexes in dogs are altered with 10 r. Kimeldorf *et al.* (7) report a radiation-induced conditioned avoidance behavior in experimental animals with a dose of 30 r.

Gross physical derangements have appeared following somewhat higher doses. Cronkite and Bond (8) report that, in man, the central nervous system form of radiation death follows a single dose of 5,000 r delivered to the head or whole body. It is in this area that it becomes particularly apparent that the consequences of a given dose depend greatly upon the manner in which it is administered. If single

¹ From the Departments of Anatomy and Radiology, The University of Texas Southwestern Medical School, Dallas, Texas. Presented at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

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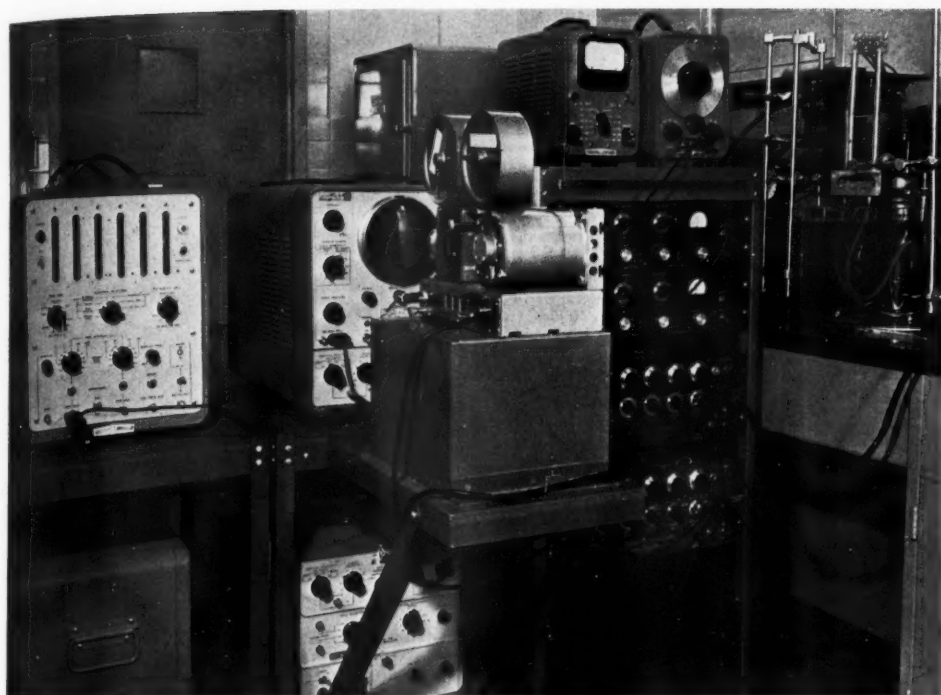


Fig. 2. Experimental equipment utilized in the neurophysiological study of the effects of radiation on mammalian peripheral nerves.

doses are given, the dose is inversely proportional to the time of appearance of clinical symptoms, and directly proportional to their severity. As one might expect, fractionation permits administration of a higher cumulative dose before these clinical symptoms occur. Boden's work (9) illustrates these inter-relationships well. On the basis of his own experience with cases of post-irradiation myelitis and reports from the literature prior to 1950, he formulated graphically the relationship between the duration of treatment and the accumulated dose in the manner of the Strandqvist time-dose relationship diagram for skin neoplasms. Figure 1, from Murphy's *Radiation Therapy* (10), was patterned after Boden. It was recommended by Boden that the central nervous system should not be submitted to a dose greater than 3,500 to 4,500 r in seventeen days, depending on the field size. At higher doses, degenera-

tion of previously healthy tissue is likely to occur. The upper diagonal line on the graph depicts the maximum safe time-dose combinations for small-volume therapy, the lower line those for large-volume therapy. Lampe (11) has subsequently reviewed this work and reported that his own results are in satisfactory agreement with Boden's limits.

Far less is known regarding the effects of moderate doses of x-rays on mammalian peripheral nerve. Published studies (12, 13) have dealt largely with the acute effects of large doses of radiation on nonmammalian nerve. In 1942, Janzen and Warren (14) reported that exposure of the peripheral nerves of rats to 200-kv x-rays in doses up to 10,000 r produced no demonstrable histologic or physiologic changes. However, these investigators performed their physiologic studies without the benefit of the sensitive electronic instruments now available for neurophysi-

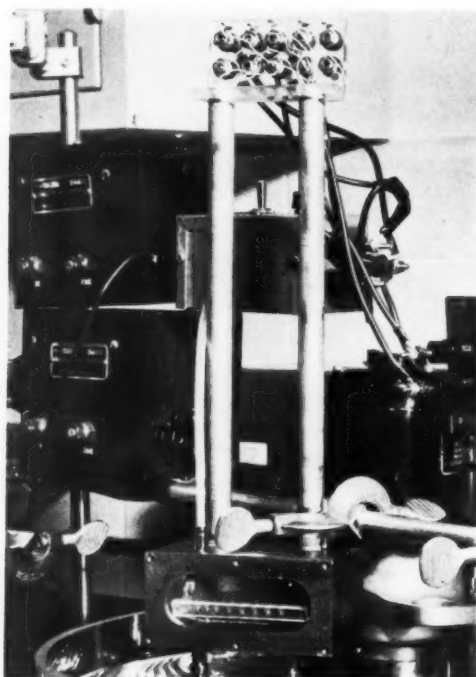


Fig. 3. Nerve chamber utilized in this study.

ologic experimentation. The mounting evidence that the central nervous system is far more radiosensitive than previously supposed and the paucity of information regarding the effects of moderate doses of radiation on mammalian peripheral nerve prompted the initiation of experiments in our laboratory in the latter field. In brief, 1,000 or 3,000 r of 250-kv x-rays were delivered to one hind limb of anesthetized cats in a single exposure. One to seven days later, the irradiated saphenous nerve was removed from the animal and submitted to neurophysiologic testing. The electronic stimulators, amplifiers, and cathode ray oscilloscope used for this purpose are shown in Figure 2, and the chamber in which the nerve is mounted for testing, in Figure 3. After a Lucite face plate is secured to the chamber, it is lowered into the water bath, which is maintained at 37° C. Figure 4 shows a closer view of the interior of the chamber and the platinum electrodes on which the nerve rests.

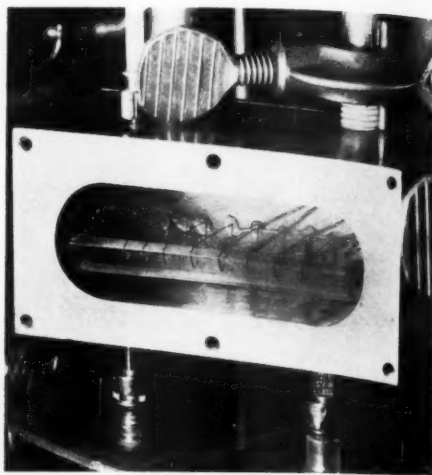


Fig. 4. Nerve chamber, showing platinum electrodes on which the nerve rests.

Control nerves for this series have been of two types: an intra-animal control nerve from the unirradiated hind limb of each of the aforementioned animals, and extra-animal control nerves from totally unirradiated animals.

It was found that the irradiated nerves developed subnormal action potentials when compared with the unirradiated control nerves, indicating that conduction in the nerve trunk had been altered. Figure 5 shows oscilloscope tracings of nerve action potentials which illustrate this depression. Their recovery processes following activity were impaired as well. These neurophysiologic studies dealt with the largest fibers of the saphenous nerve: those myelinated fibers which have conduction velocities between 60 and 80 meters per second. Investigations are at present under way to test in the same manner the smaller pain fibers of the saphenous nerve. In view of past and present controversies regarding the place of x-ray therapy in painful conditions such as bursitis, it will be of both academic and clinical interest to ascertain whether or not the pain afferents are similarly depressed.

Although the main emphasis of our experiments has been focused on the bioelectrical activity of the nerves, a func-

tional derangement was also noted. Some animals receiving a single exposure of 3,000 r to one leg showed impairment of the righting reflex when dropped from an intermediate height. Instead of landing with agility, as they did prior to irradiation, they were clumsy, generally falling to one side.

SUMMARY

Some of the more pertinent work in the area of neuroradiobiology has been reviewed. Recent investigations have yielded new information in this long neglected area. Some of this has been summarized in Tables I and II. These show the smallest single dose of radiation of various common qualities which has been found to produce the derangements

TABLE I: LOWEST SINGLE DOSES OF RADIATION FOUND TO PRODUCE STRUCTURAL CHANGES IN THE MAMMALIAN NERVOUS SYSTEM

Subependymal cells.....	200 r
Myelin.....	1,200 r
Neurons.....	1,200 r
Oligodendroglial cells.....	1,200 r

TABLE II: LOWEST SINGLE DOSES OF RADIATION FOUND TO PRODUCE FUNCTIONAL CHANGES IN THE MAMMALIAN NERVOUS SYSTEM

Brain bioelectrical waves.....	0.05 r
Conditioned reflexes.....	10 r
Conditioned avoidance behavior.....	30 r
Depressed peripheral nerve activity.....	1,000 r
Central nervous system damage.....	1,500 r
Spinal cord reflex changes.....	5,000 r
Central nervous system radiation death.....	5,000 r

listed. As for structural changes, the subependymal cells of the lateral ventricles have been affected by the lowest dose. With regard to functional changes, behavioral modifications have occurred at extremely low doses, and other parameters of activity have been affected by moderate doses.

The concept of the radiation tolerance of the nervous system has undergone a phasic development. Early histologic studies detected no structural derangements with large doses and, because of limitations in instrumentation, physiologic changes were not found. Hence, nervous tissue was deemed highly radioresistant. The overconfidence fostered by this view has

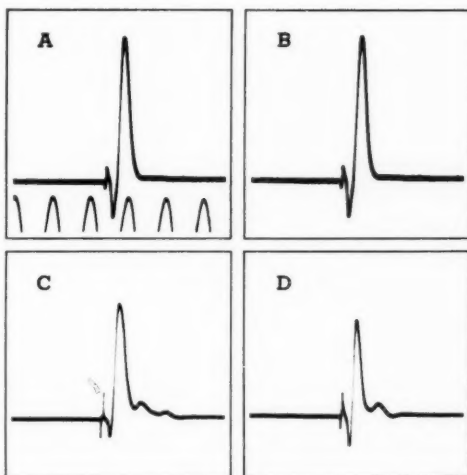


Fig. 5. Action potentials of cat saphenous nerves. A and B. Recordings from right and left saphenous nerves of unirradiated control animal. Tracings are nearly identical.

C. Recording from unirradiated saphenous nerve from cat 14.

D. Recording from irradiated saphenous nerve from cat 14, showing depressed performance in comparison with the unirradiated moiety from the same animal.

Time signal of 1,000 cycles used for all recordings. Peak-to-peak distance on time line also equals 5 mv in vertical direction. These, and some of the other recs, exhibit an initial positivity which can be considered as a triphasic artefact due to the method of grounding. This positivity was not always present, and did not influence ratios of spike heights.

ironically been instrumental in abrogating it. The many reports of clinical derangements following therapeutic doses previously thought safe have contributed in no small way to the reassessment of the radiation tolerance of the nervous system.

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SUMMARIO IN INTERLINGUA

Le Effecto de Radiation in Nervos Mammalian

Esseva effectuate appropriateamente controlate studios in re le radiosensibilitate de nervo peripheric mammalian. Doses de 1.000 e 3.000 r de radios X de 250 kv esseva delivrate a un del gambas posterior de anesthesiate cattos in un sol exposition. Inter un e septe dies plus tarde, le irradiate nervo saphen esseva removite ab le animal e subjicite a tests neurologic. Le observationes esseva restringite al fibras le plus grande del nervo, i.e. le myelinate fibras

que ha un velocitate de conduction de inter 60 e 80 metros per secunda.

Esseva trovate que le irradiate nervos, disveloppava subnormal potentiales de action, lo que indica un depression del conduction in le trunco nerval. Le processo de recuperation esseva etiam disturbate. In plus, un certe disrangiamento functional esseva notate. In vista de iste e altere studios, le concepto del tolerantia irradiatori del systema nervose es sub re-evaluation.

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The Latent Period, Incidence, and Growth of Sr^{90} -Induced Osteosarcomas in CF1 and CBA Mice¹

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INVESTIGATIONS of the carcinogenic response of laboratory animals to ionizing radiation, either externally or internally applied, are usually focused upon the neoplasms present at death. Consequently the morbidity data are very closely bound to the mortality data, an association that is often overlooked. However, an appreciation of the fact that the true incidence of a disease may be quite different from its apparent incidence at death does not automatically solve the problem of separating morbidity from mortality, because in most instances the recognition of neoplastic disease must wait until the mass can be palpated, or until necropsy. A notable exception is the malignant bone lesion, which can be detected roentgenographically in the living animal long before it can be palpated.

The objectives of the present investigation, employing periodic x-ray examination of the skeletons of mice that had received radiostrontium, were: (a) to study the development of osteosarcoma as a disease apart from mortality, (b) to follow the growth of individual tumors from their first roentgenographic identification to the death of the host, and (c) to compare the radiocarcinogenic responses of two distinct strains of mice. Each of these aspects of the investigation is pertinent to the problem of latent period, which is one of the very intriguing but poorly understood characteristics of tumor induction.

MATERIALS AND METHODS

Sr^{90} , in equilibrium with Y^{90} , was injected intravenously into 29 CF1 and 24 CBA female mice approximately seventy days old. The former received an average of $0.9 \mu\text{c/gm. body weight}$ (range, 0.81 to $1.03 \mu\text{c/gm.}$) and the latter an average of

$1.1 \mu\text{c/gm.}$ (range, 0.96 to $1.23 \mu\text{c/gm.}$). This amount of Sr^{90} is known to produce a high incidence of osteosarcoma (1).

Roentgenograms were taken one month after injection, at two- to four-week intervals during the next two months, and weekly thereafter. The final picture was obtained at autopsy. Exposure required three-quarters of a second at 30 ma and 32 kv 19 inches from the tube. The radiation received by the mice from this procedure was insignificant compared with that derived from the $\text{Sr}^{90}\text{-Y}^{90}$. By retrospective examination of the roentgenograms, the sarcomas present at death could be traced back to their first appearance. It was sometimes difficult to determine the earliest film of a specific lesion with definite neoplastic characteristics, and some lesions persisted in an apparent nonmalignant state for many weeks. If the integrity of the cortex was interrupted, malignancy was diagnosed. In a few instances the cortex was intact, but the general appearance of the lesion favored a diagnosis of malignancy. Examination of the films with a magnification of $\times 7$ was helpful in the case of some of the very small lesions, since the benefits of this degree of enlargement were not negated by excessive increase in film graininess.

Estimates of tumor volume were based on the apparent areas as seen on the roentgenograms. Often the noncalcified portion of the tumor could be discerned, but if the periphery of the mass was not clear, its location was approximated. The volumes of tumors with areas of 0.4 sq. cm. or more, as measured planimetrically, were calculated on the assumption that the masses were spherical. Smaller tumors were assumed to be oblate spheroids, and their volumes were estimated from the

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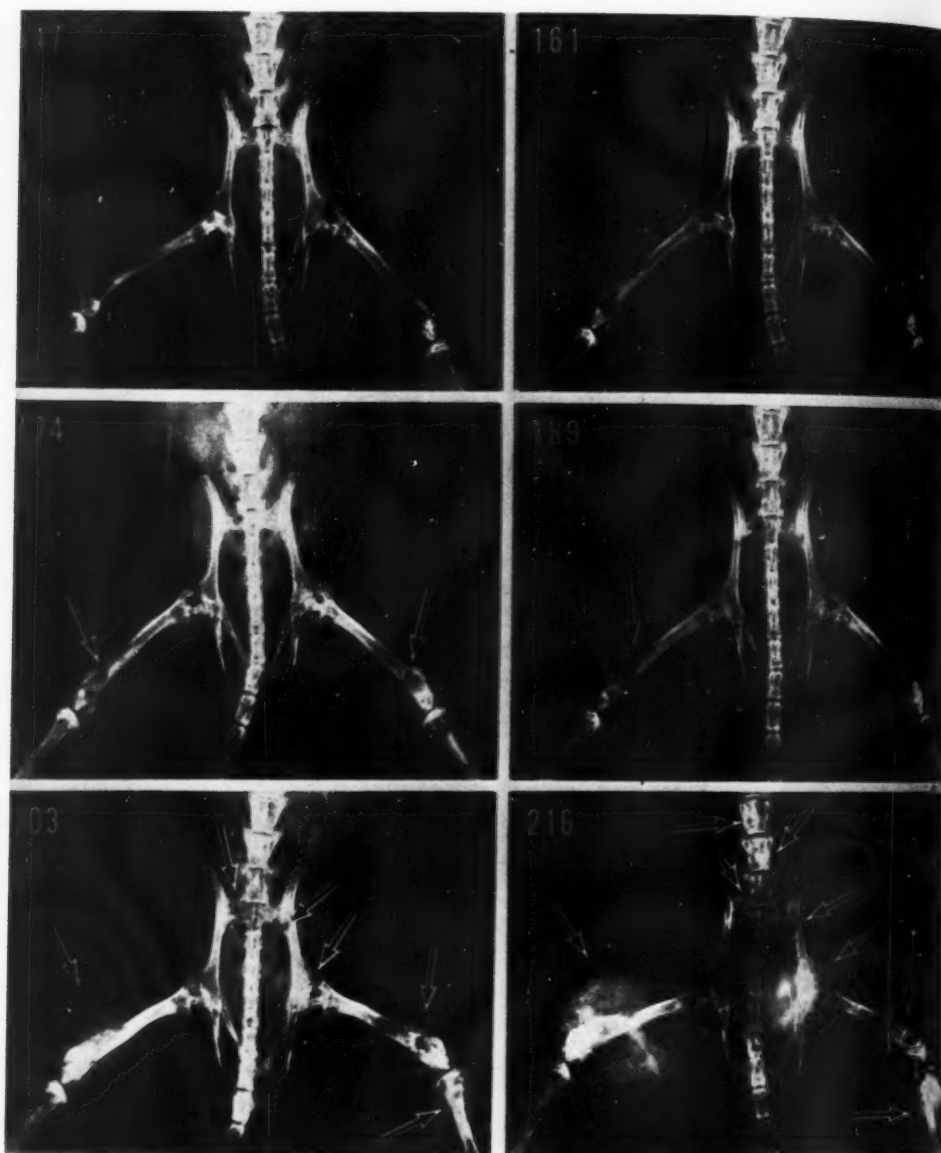


Fig. 1. Roentgenograms of CF1 mouse No. 49. The numbers refer to days after injection. Arrows indicate the osteosarcomas. Additional tumors were located in the first cervical and fifth thoracic vertebrae.

longest and shortest diameters measured on the x-ray film.

The roentgenographic series shown in Figures 1 and 2, which include only a few of the films in each sequence, illustrate the type of material upon which the study was based. Although it was not hard to

assess the malignancy of most of the terminal lesions, setting the time of malignant change was in many cases quite difficult. Decisions were greatly facilitated by back-and-forth comparisons with previous and subsequent pictures. Doubtless many errors have been made, but they

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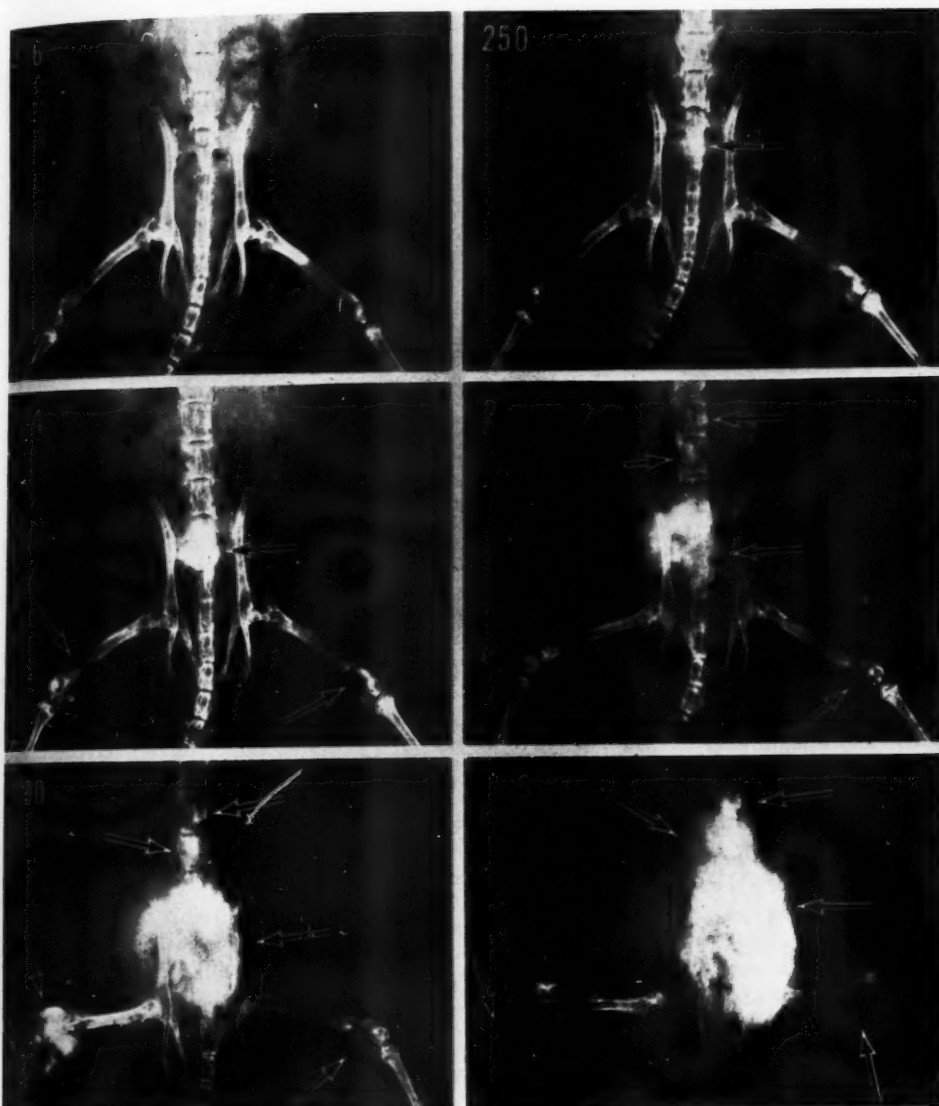


Fig. 2. Roentgenograms of CBA mouse No. 13. The numbers refer to days after injection. Arrows indicate the osteosarcomas.

should be consistent since all judgments regarding malignancy were the responsibility of one individual.

Similarly, errors in defining the spatial limits of the osteosarcomas should be consistent. The rate of growth of individual tumors varied greatly, as is evident in the illustrations. For example, in Figure 1 the tumor of the right distal femur grew

from 0.002 c.c. one hundred and seventy-four days after injection to 2.3 c.c. at two hundred and sixteen days, an increase of over a thousandfold in six weeks. In contrast, the tumor of the left distal femur grew from 0.013 c.c. at one hundred and sixty-one days to 0.118 c.c. at two hundred and sixteen days, which was less than a tenfold increase in eight weeks.

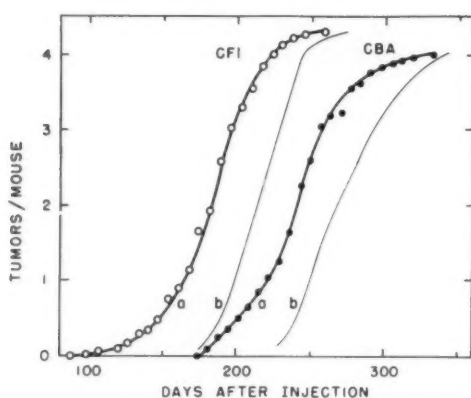


Fig. 3. Cumulative incidence of osteosarcomas. *a.* Morbidity incidence. *b.* Morbidity-mortality incidence.

RESULTS

Tumor Incidence: One hundred and twenty-five osteosarcomas were identified roentgenographically among the 29 CF1 mice, and 96 among the 24 CBA mice. The difference between the average number of tumors per mouse in the two strains, 4.31 ± 0.35 (standard error) for the former and 4.00 ± 0.45 for the latter, was not statistically significant. The actual number of tumors per mouse ranged from none (1 animal) to ten (1 animal), the mode being three. Since the distribution of tumors among the 53 mice was not significantly different from a Poisson distribution, there is no indication that the presence of one tumor influenced the development of a second or that some animals were either especially tumor-susceptible or especially tumor-resistant.

The cumulative incidence of tumors in each strain is given in Figure 3. The earliest positive diagnosis was made in a CF1 mouse ninety-eight days after injection and in a CBA mouse one hundred and eighty days after injection. A difference in time persisted, and the CBA "a" curve lags behind the CF1 "a" curve by approximately sixty days. However, the shapes of the two morbidity incidence curves, which give the incidence of osteosarcomas at the time of diagnosis, are remarkably similar. For comparative purposes, the incidences of tumors at

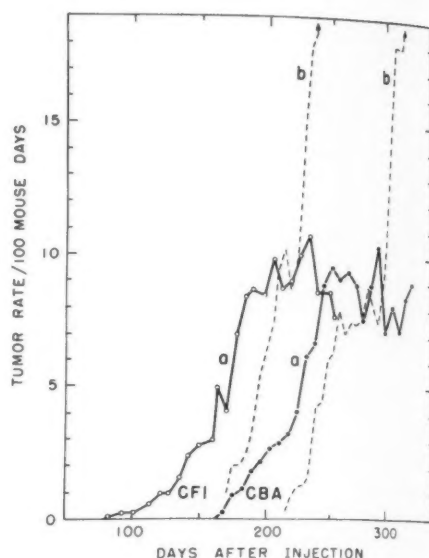


Fig. 4. Tumor rate/100 mouse days. *a.* Morbidity rate. *b.* Morbidity-mortality rate.

death ("b") are also presented. The difference in time between the morbidity and the morbidity-mortality curves of each strain is about thirty days over the range covered by 1 to 3 tumors per mouse.

Tumor Rate: The rate of appearance of osteosarcomas per hundred mouse days is presented in Figure 4 as a function of time after injection. The plotted values were obtained by dividing the number of tumors appearing for the first time during a four-week interval by the number of mouse days lived during that interval. The calculation was repeated every week. The curves for the two strains are very similar when the CBA values are moved sixty days to the left. It should be noted that the morbidity rates did not continue to increase as time went on. Instead, they reached a plateau that was more or less maintained until most of the mice had died. This is contrary to the usual situation in which tumor rate calculated at the time of death continues to increase as long as a reasonable number of individuals remains. The curves in Figure 4 labeled "b," which are based on tumor rate at death, illustrate this point.

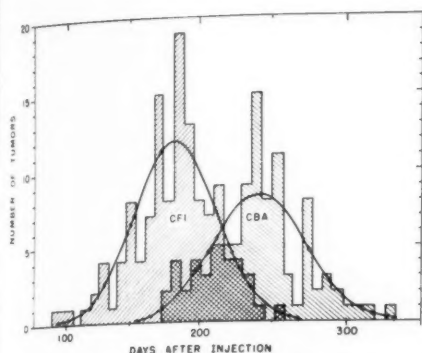


Fig. 5. Frequency distribution of osteosarcomas as a function of time after injection.

Tumor Frequency: In Figure 5 each osteosarcoma is represented at the time when it was first diagnosed. With the exception of their mean times, the parameters of the frequency distributions of the two strains are very similar. The difference in peak frequency is due to the fact that there were 125 CF1 tumors but only 96 CBA tumors. The average time of appearance of the CBA tumors was 244.3 ± 3.3 days, which was 61.9 days later than the 182.4 ± 2.6 days average for the CF1 tumors. The derived normal frequency distributions are also indicated in Figure 5. The Chi-square test of the difference between the observed distribution and the calculated distribution gives a probability of 20 to 30 per cent that the CF1 data represent a random variation from a normal distribution. The probability for the CBA data is 5 to 10 per cent, Chi square being 19.45 with 12 degrees of freedom and the 5 per cent probability level being 21.03.

Tumor Location: The anatomical location of each tumor is indicated in the frequency distributions in Figure 6. There was no indication in either strain that tumors appeared sooner in one bone than in another or that the location was in any way associated with time after injection. The proportion of tumors occurring in various body regions is presented in Figure 7. The differences between the two strains were tested by the Chi-square method and found to be insignificant since the prob-

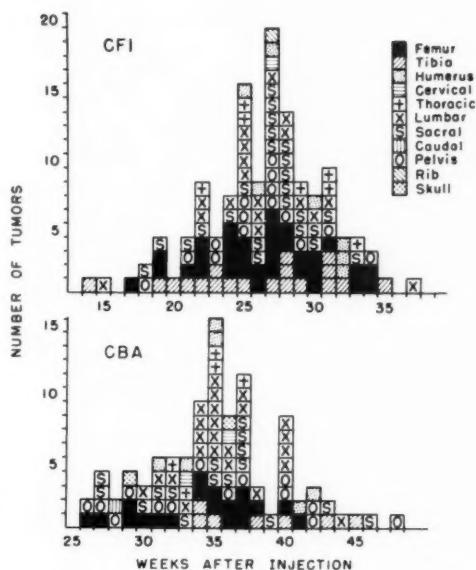


Fig. 6. Frequency distribution of osteosarcomas by anatomical location as a function of time after injection.

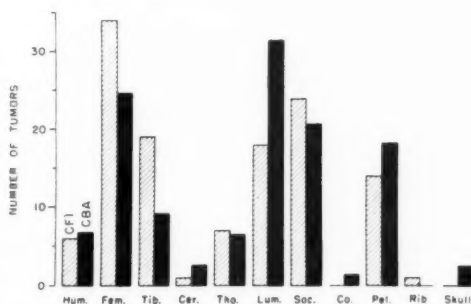


Fig. 7. Anatomical distribution of tumors (number normalized at 125/strain).

ability is 10 to 20 per cent that the observed variations are due to sampling error. The greatest contribution to Chi square comes from the lumbar tumors, but when the proportions of these tumors alone are compared, the difference is still not statistically significant. In neither strain was there a statistically significant difference between the number of tumors on the right and left sides of the body.

Tumor Occurrence Relative to Dose: The preceding information combined with some recent measurements of the radiant energy absorbed by the mouse skeleton provides

a means of evaluating the relative contributions of the total accumulated dose and the dose rate to the carcinogenic response. In Figure 8 the dose delivered by $\text{Sr}^{90}\text{-Y}^{90}$ to a $10\ \mu$ cell in the femur of a seventy-day old CF1 mouse is plotted as a

epiphyseal plate. To facilitate comparison, the tumor rates illustrated in Figure 4 have been repeated. These were selected rather than the frequency distributions because of their inherent correction for population size.

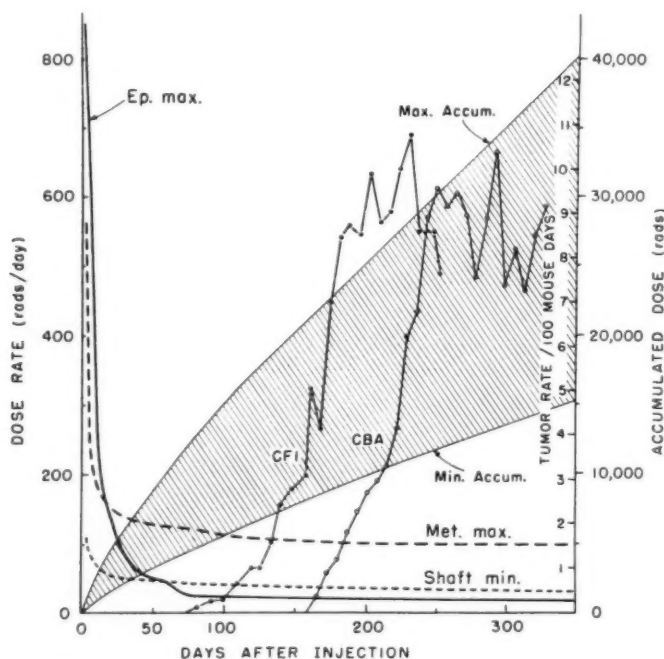


Fig. 8. Dose rate and total dose delivered to a $10\ \mu$ cell in a mouse femur from an intravenous injection of $1\ \mu\text{c}\ \text{Sr}^{90}/\text{gm.}$ body weight at seventy days of age, as a function of time after administration. The maximum dose rates in the distal epiphyseal plate and in the metaphysis and the minimum dose rate in the shaft are compared to the total accumulated dose expressed as the range between the maximum in the metaphysis and the minimum in the shaft. The tumor rates of Figure 4 serve as points of reference.

function of time after the injection of $1.0\ \mu\text{c}/\text{gm.}$ body weight. The values were derived from Figures 18 and 31 of the report on dosimetry in the mouse skeleton by Marshall and Finkel (2). The femur serves well as a representative bone for this comparison, but it should be understood that the situation throughout the skeleton is not identical to that in the femur. The accumulated dose is presented as a range with the maximum in the distal metaphysis as the upper limit and the minimum in the mid-shaft as the lower limit. Daily dose rates are given for these two locations as well as for the distal

Two points relative to the accumulated dose deserve special attention. (a) In spite of the continuing increase in the total energy absorbed, the morbidity rates remained relatively constant after their initial increase. A correlation between these two indices could not be demonstrated. (b) The average CBA mouse accumulated between 2,000 and 6,000 rads more than the average CF1 mouse, but, except for the difference in time, the carcinogenic responses of the two strains were remarkably similar. The number of tumors at death was not associated with the time of death when the two populations

were examined together or when the CF1 mice were examined alone. However, in the CBA population there was an increase of 0.029 ± 0.011 tumor/day, with only 1 chance in 100 that a zero slope would have a similar deviation. When the last mouse dying at three hundred and forty-two days was omitted from the calculations, the slope was 0.030 ± 0.013 tumor/day, and the probability increased to 2 to 5 per cent that a zero slope would have a similar deviation. Exclusion of the last 2 survivors, dying at three hundred and sixteen and three hundred and forty-two days, changed the probability to between 5 and 10 per cent. There is thus an indication that the accumulated dose may have contributed at least in some small measure to tumor induction.

The relegation of the accumulated dose to a very minor role in tumor induction in this experiment directs attention to the dose rate, which was maximum immediately after injection but decreased very rapidly thereafter. It is possible that the necessary stimulus was delivered well within the first ten days, during which period the initial doses in the epiphyseal plate and in the metaphysis, for example, dropped from approximately 850 and 550 rads/day, respectively, to 250 and 180 rads/day, respectively. On the twentieth day after injection the distal epiphyseal plate was receiving approximately 130 rads/day and the maximum dose being received by the metaphysis was approximately 150 rads/day.

Tumor Growth: The individual CF1 tumors could be followed for an average of 5.55 ± 0.28 weeks and the CBA tumors for 5.51 ± 0.27 weeks. The frequency distribution of tumors as a function of number of weeks from their first appearance until death of the host followed a normal pattern. Ten tumors were observed either only at death or within three days of death, 18 were followed for at least ten weeks, and 1 had been present for eighteen weeks by the time the animal died.

Four of the total 221 osteosarcomas

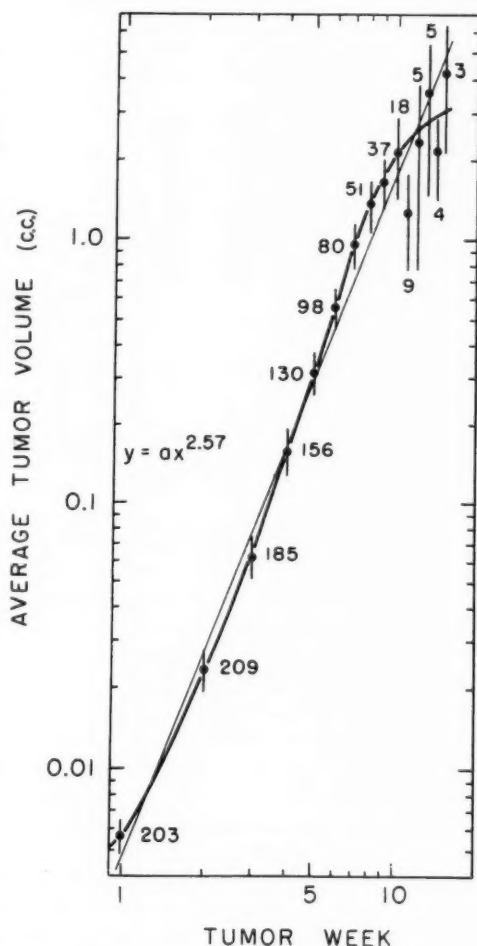


Fig. 9. Average tumor volume as a function of time after x-ray diagnosis. The vertical lines include one standard error of the mean. Numbers refer to number of tumors determining each mean.

could not be included in the study of tumor growth because they were very small and their boundaries remained obscure. A few other tumors could not be measured when they first appeared but were followed quite readily thereafter. The 217 measurable tumors provided 1,196 measurements, an average of 5.5 per tumor.

The mean volume of the CF1 tumors was 0.0060 ± 0.0012 c.c. when they were first observed (week 1) and 2.246 ± 1.195 c.c. nine weeks later (week 10). The CBA tumors averaged 0.00513 ± 0.00090 c.c. at

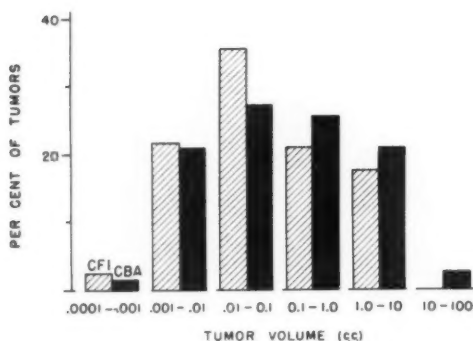


Fig. 10. Frequency distribution of osteosarcomas according to size at the time of death of the host.

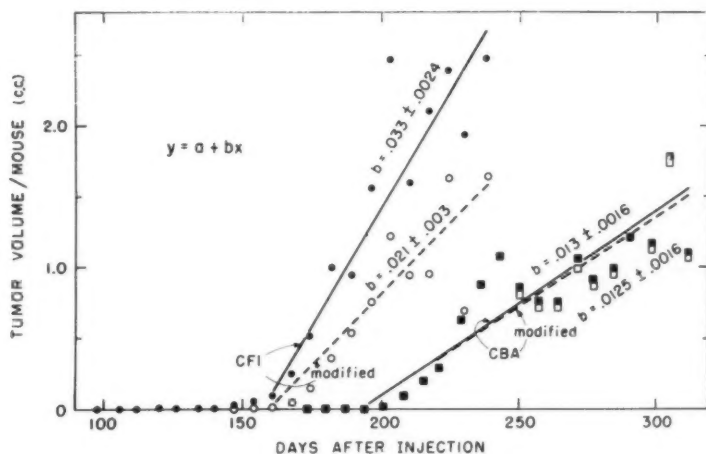


Fig. 11. Total tumor mass in the living population, expressed as volume per mouse, as a function of time after injection. The "modified" volumes exclude those tumors located in the thoracic and lumbar spine and in the tibia.

one week and 1.977 ± 0.774 c.c. at ten weeks. Since the differences in the means of the tumor volumes in the two strains at any week were not statistically significant, the data from the two populations were combined. In Figure 9 the average tumor volume at successive weeks after first positive diagnosis is plotted on a log-log scale. The regression line, $y = ax^{2.57}$, fits the data reasonably well, but the pattern of positive and negative differences suggests that an S-shaped function would fit even better and that growth might not have been as rapid before the tumors were roentgenographically recognizable.

The rate of growth of the osteosarcomas

in various anatomical sites was compared to the average rate of growth. Among the CF1 tumors, those in the thoracic spine grew somewhat more slowly and those in the sacral spine and humerus grew somewhat more rapidly than the average, but the differences were not statistically significant. Among the CBA tumors, however, those in the thoracic and lumbar spine and in the tibia grew significantly slower than the average. The value of the exponent of x was 1.69 for the thoracic tumors, 0.633 for the lumbar tumors, and 1.13 for the tibial tumors. In each in-

stance the probability of the difference from the average being due to chance was 1 or less than 1 in 1,000. Comparisons of the rate of growth of tumors on the right and left sides of the body showed no significant differences.

The frequency distribution of the tumors according to size at the time of death of the host followed a lognormal pattern (Fig. 10). The difference between the geometric means of the two strains, 0.099 c.c. for the CF1 tumors and 0.062 c.c. for the CBA tumors, is not statistically significant.

Population Aspects of Tumor Growth: In the preceding discussion of tumor

growth the time axis was normalized according to tumor age, week 1 for each osteosarcoma being the time when that tumor was first diagnosable. A somewhat different approach provides information pertaining to the growth of the total tumor mass within the population. In Figure 11 the sum of all the tumor volumes in the surviving population divided by the number of surviving individuals, or the average tumor volume per living mouse, is plotted against time after injection. Since the CBA thoracic, lumbar, and tibial tumors grew significantly more slowly than the other tumors, the total tumor mass per mouse in each population was calculated both with and without the tumors in these locations. Their exclusion changed the CBA values very little, but it significantly decreased most of the CF1 values.

Regression lines were fitted to the CF1 and CBA data after one hundred and sixty one and one hundred and ninety-four days post-injection, respectively, until only 2 or 3 mice remained alive. These origins were selected because they provided the smallest standard errors. The difference between the slopes of the CF1 and CBA lines is greatly diminished when the thoracic, lumbar, and tibial tumors are omitted, but it remained statistically significant since $P=0.03$.

The scale of the y-axis has been increased in Figure 12 so that the early growth of the total tumor mass can be illustrated. Exclusion of the three atypical tumor sites changed the CF1 but not the CBA values during this period. The double logarithmic regression lines calculated from the three sets of values are quite different, and the exclusion of the thoracic, lumbar, and tibial tumors does not greatly decrease the dissimilarity between the two strains.

DISCUSSION

Studying the development and growth of osteosarcomas by means of successive x-ray films proved to be a very satisfactory method. In spite of the irreducible sources of error associated with making positive

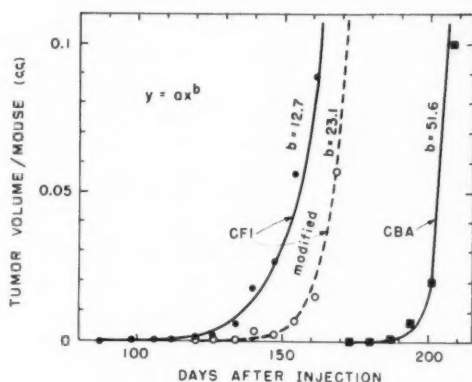


Fig. 12. Total tumor mass from 0 to 0.1 c.c./mouse in the living population as a function of time after injection.

diagnoses of malignant growth and absolute measurements of tumors from roentgenograms, the data were surprisingly consistent.

The difference between tabulating tumor incidence at the time of roentgenographic appearance and at the time of death was primarily a difference of thirty days on the time axis. However, calculating tumor rate at the time of x-ray diagnosis and at the time of death resulted in very dissimilar pictures of morbidity rate. Instead of the usual increase in rate with increasing time, the rate of roentgenographic appearance of osteosarcomas reached and remained at a plateau. Although there is often a valid reason, or a real necessity, to present morbidity rate at the time of death rather than at the time the disease appears, the latter is much more pertinent to problems of carcinogenesis. This is particularly true when one is seeking to identify an unknown carcinogen or to determine the amount of a known carcinogen required to produce neoplastic change. If the tumor is rapidly and unequivocally lethal, the difference between the morbidity and the morbidity-mortality rate will not be great. In the present experiment, although a bone tumor was the primary cause of death in almost every instance, most of the osteosarcomas were merely incidental to rather than contributory to death. In populations subjected

to smaller amounts of radiostrontium, on the other hand, the majority of deaths are due to causes other than bone tumor (1). It is not surprising, then, that the rate of mortality with a neoplasm does not accurately reflect the rate of its appearance. Furthermore, the true morbidity rate, which will be known only when our diagnostic methods permit positive identification of malignant change as soon as it occurs, is probably quite different from the rate of earliest roentgenographic detectability of the neoplasm.

The carcinogenic responses of the two strains of mice were strikingly similar in most respects. However, the CBA's required about sixty days more than the CF1's for the response to be manifest. The explanation is not apparent and, since these are two strains of the same species, one cannot call upon such factors as body size and life span.

One of the most perplexing problems in radioisotope carcinogenesis is the assessment of the absorbed dose responsible for the neoplastic change. Unlike irradiation from an external source, which can be regulated to produce a known amount of ionization at a given location and can be turned on and off at will, the internal emitters deliver different amounts of energy to different sites and to the same site at different times, depending upon a number of physical and biological factors that can be controlled only to a limited extent. The present experiment provides some data pertinent to this problem. The fact that the frequency distribution of tumors as a function of time after injection followed a normal pattern in each strain suggests that the time of induction was constant but that tumor development time was variable. This hypothesis does not conflict with the observed strain difference. If, on the other hand, the induction time varied and development time was constant, a normal frequency distribution hardly could have resulted and the sixty-two-day difference between the two strains in average time to tumor detection could not be explained. A third possibility is that

the time of radiation stimulation was constant but a second event, which occurred with a normal frequency distribution and averaged sixty-two days later in the CBA's than in the CF1's, was required before the neoplastic process could proceed.

The tumor-rate data suggest that the major carcinogenic stimulus had been received some time before the first tumor appeared, since a statistically significant correlation could not be demonstrated between morbidity rate and total dose. There was, however, a correlation between time of death and number of tumors at death among the CBA mice. This correlation ceased to be significant when the last two survivors were omitted, but the implication remains that the accumulated dose was not entirely ineffectual. Even so, the total dose cannot explain the close agreement between the rates in the two strains because their time scales differed by about sixty days, and total accumulated dose increased with time after injection. The best evidence in support of the total dose as the carcinogenic agent comes from an experiment involving the continuous ingestion of radiostrontium (3). Mice that had been exposed since conception to a diet containing $10 \mu\text{C}$ Sr^{90}/gm . Ca did not die with osteosarcomas until after they were four hundred and fifty days old. A definitive statement cannot be made because the dosimetry in this case has not yet been examined carefully, but tumor induction may have been associated with the total dose rather than with the dose rate.

Since the total accumulated dose seems to have been relatively unimportant in inducing osteosarcomas in the present experiment, the dose rate soon after injection must have provided the major stimulus. A rough estimate of the required dose rate can be obtained by considering together the dose measured in the femur at various times after injection and the incidence of tumors as a function of the amount of material injected. For this purpose a comparison can be made between the 4.3 tumors/CF1 mouse observed in this

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experiment and the 0.15 tumor/CF1 mouse seen after the injection of 0.2 μ c Sr⁹⁰/gm. in a previous experiment (1). In the former instance it can be assumed that most of the tumors resulted from a dose rate similar to the maximum in the femoral metaphysis, which decreased in ten days from 550 to 180 rads/day and in twenty days to 150 rads/day. In the latter case the femoral metaphysis received a maximum of 125 rads/day for a very short time, during the first day. By the end of that day the maximum dose rate in the metaphysis was only 90 rads/day, and at ten days it was 36 rads/day. With the smaller injection, the only area of the femur receiving a higher dose rate was the epiphyseal plate, which received 170 rads/day immediately after injection and 150 rads/day as an average throughout the first day. The rate ten days after injection had decreased to 50 rads/day. If the same critical dose rate is required at both injection levels, the decreased carcinogenicity of the lower dose can be ascribed to the fact that only a small portion of the skeleton received sufficient radiation to evoke neoplastic change. If this hypothesis is correct, dose-response curves should be interpreted on the basis of the amount of potentially reactive tissue receiving the critical dose rate rather than upon the average dose to the entire skeleton. These considerations, along with the evidence that the accumulated dose is relatively unimportant, suggest that a dose rate in the mouse skeleton of less than 150 rads/day is ineffective as a carcinogenic agent.

It had been hoped that the tumor growth data would provide a means by which zero tumor time and minimum tumor size could be estimated. Although the regression of tumor volume against tumor time fits the power function $t^{2.57}$ reasonably well, the fit is not quite good enough to permit extrapolation, because a log-log plot of the data is slightly S-shaped instead of straight. That is, the growth rate decreased with decreasing time from three weeks to one week, and it is likely that the

rate was even slower before the tumors were detected. Therefore, until a reliable mathematical expression can be assigned to this early portion of the curve, prediction of zero tumor time and initial tumor size is not possible. The smallest tumor measured on the roentgenograms had an estimated volume of 0.00011 c.c. This volume could contain about 200,000 cells, each with a diameter of 10 μ . The present data do not furnish a clue as to whether a tumor originates in one cell or in a group of cells. It is hoped that extension of the growth curve to the left by the use of more refined techniques will be possible, and that the information required for extrapolation will then be provided.

The growth of osteosarcomas seems to proceed through at least three stages. The initial phase is concerned with establishment and adjustment to the environment; the second phase, from about three to seven weeks after roentgenographic diagnosis, is the period of rapid expansion under optimum conditions; the third phase represents retardation due probably to such factors as inadequate blood supply, lack of space into which to extend, or general debilitation of the host. There is no apparent explanation for the slower growth of the thoracic, lumbar, and tibial tumors in the CBA mice. Perhaps there is a physiological difference in these areas between the strains and between these and other areas within the CBA mouse.

The major difference in the carcinogenic response of the CF1 and the CBA mice was the time of roentgenographic appearance of the osteosarcomas. If this result were due to a difference in the moment of neoplastic transformation, the total tumor mass within the CF1 and the CBA populations should have increased at the same rate. That is, the plots of total tumor volume/mouse against days after injection should have been parallel but separated by approximately sixty days. This result was not observed. Instead, the rate of increase in the CF1 population was significantly greater even when the tumors in those locations that grew more slowly in

the CBA mice were excluded. Since there was not a significant difference between the strains in tumor incidence, in the dispersion of the normal frequency distribution of tumors against time, in the patterns of morbidity rate, in tumor-growth rate, or in size of tumors at the time of death of the host, the reason for the dissimilarity in the rate of increase of the total tumor mass within the populations remains obscure. It is possible, of course, that many minor discrepancies, all in favor of a greater carcinogenic response of the CF1 mice, might in combination have resulted in a statistically significant difference.

In any event, a difference in the time of neoplastic change is probably not the reason for the sixty-day discrepancy between the two strains. The answer might be found by studying the incidence of tumors before they are recognizable by radiography. An attractive hypothesis is that the newly transformed neoplastic cell or group of cells finds a much more favorable environment in the CF1 mouse than in the CBA mouse. As a consequence, the CF1 tumors become established more rapidly and reach the phase of maximum growth sooner than the CBA tumors. The CBA tumors, once they overcome the resistance of the host, display the same growth pattern as the CF1 tumors. This hypothesis assumes that the tumors in the two strains are the same but that the average CF1 and CBA mouse have different degrees of resistance to the initial stages of tumor development. In addition, since tumors appear at different times among mice of the same strain, it is possible that individual mice have different degrees of resistance to the establishment and growth of the neoplasms that have been induced.

SUMMARY

1. CF1 and CBA mice were injected intravenously with a potent carcinogenic amount of Sr^{90} ($1.0 \mu\text{c/gm.}$), after which the appearance and growth of osteosarcomas were studied by serial roentgenography.

2. The osteosarcomas were distributed

at random among the mice, the average number being 4.3 among the CF1 and 4.0 among the CBA mice.

3. Tumor incidence recorded at the time of x-ray diagnosis was similar to the incidence recorded at the time of death except that it preceded the latter by about thirty days. However, tumor rate recorded at the time of x-ray diagnosis was very different from the rate recorded at the time of death. The former reached and remained at a plateau; the latter increased until the populations were small.

4. Except for the fact that almost all events occurred about sixty days later among the CBA mice, the tumor data for the two strains were much alike.

5. The tumor data considered along with data on absorbed dose indicate that in this experiment the accumulated dose was relatively unimportant as a carcinogenic stimulus and that the dose rate during the first days after injection provided the amount of radiation necessary to induce malignant bone tumors. It is suggested that 150 rads/day for only one day might approximate the required amount. It is also suggested that dose-response curves reflect the volume of tissue that receives the critical amount of radiation.

6. The average rate of growth of all the tumors for ten weeks, starting with the week of the first positive x-ray diagnosis, followed the power function, $t^{2.57}$.

7. The total mass of neoplastic tissue increased more rapidly in the CF1 than in the CBA population. Consequently, the difference in time of tumor appearance in the two strains, as determined roentgenographically, cannot be attributed to differences in the moment of neoplastic change. It is suggested that the CBA host might provide a less favorable environment for the early establishment and growth of an osteosarcoma than the CF1 host.

ACKNOWLEDGMENT: The authors are greatly indebted to Mr. Merlin Dipert for processing the tumor growth data through an electronic computer.

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DISCUSSION

Henry Kaplan, M.D. (Palo Alto, Calif.): I think this is an extremely interesting set of data. The only thing I would question is the last interpretation about the resistance of mice. "Resistance" ordinarily connotes some sort of immunologic mechanism. I don't know if there is any evidence in induced sarcomas of immunologic differences between the host and the autochthonous tumor. In this instance there is certainly an alternative postulate which I would find more attractive, namely, the concept of

conditioned *versus* dependent states and the possibility that in early stages of tumor development the response of the bone tumor cells is in part conditioned by hormonal or environmental factors. It is entirely conceivable, e.g., that the response of these two strains to standard doses of pituitary growth hormone might be different. I wonder if you have any data on this?

Dr. Finkel: No, we have no data on that point. It is a very interesting suggestion and one that we can pursue a little further.

SUMMARIO IN INTERLINGUA

Le Periodo de Latentia e le Incidentia e Crescentia de Osteosarcomas Inducite per Sr⁹⁰ in Muses CFI e CBA

Esseva effectuate un studio con le objectivos de (1) investigar le disveloppamento de osteosarcoma como morbo, sin riguardo al mortalitate causate per illo, (2) observar continuemente le crescentia de tumores individual ab lor prime identification roentgenographic usque al tempore del morte del hospite, e (3) comparar le responsas radiocarcinogenic de duo distincte racias de muses. Muses CFI e CBA recipeva injectiones intravenose de doses potentemente carcinogenic de Sr⁹⁰ (1.0 µc/g), e subsequelemente le apparition e le crescentia de osteosarcomas esseva studiata per roentgenographia serial.

Le osteosarcomas esseva distribuite aleatorimente inter le muses. Lor numero medie per mus esseva 4,3 in le racia CFI e 4,0 in le racia CBA. Le incidentia de tumores notate al tempore del diagnose per radios X esseva simile al incidentia notate al tempore del morte, excepte que illo precedeva lo per circa trenta dies. Tamen, le prorata de tumores notate al tempore del diagnose per radios X esseva multo differente ab le prorata notate al tempore del morte. Le prorata de mortalitate attingeva un plateau que se

manteneva plus o minus continuemente usque le majoritate del muses habeva morite.

A parte le facto que quasi omne le evenimentos occurreva circa sexanta dies plus tarde in le muses CBA, le datos pro le tumores in le duo racias esseva multo simile. Le dose accumulate esseva relativemente inimportante como stimulo carcinogenic, e il esseva le intensitate durante le prime dies post le injection que provideva le quantitate de radiation necessari pro inducer maligne tumores. Le prorata medie de crescentia de omne le tumores durante dece septimanas a partir del prime positive roentgeno-diagnose sequeva le function de potentia $t^{2.57}$.

Le massa total de tissu neoplastic cresceva plus rapidemente in le muses CFI que CBA. Per consequente, le differentia del tempores de apparition del tumor inter le duo racias secundo determinationes roentgenographic non pote esser attribuite a differentias in le quantitate del alteration neoplastic. Es suggestionate que le hospite CBA provide un ambiente minus favorable pro le establimento e crescentia de osteosarcomas que le hospite CFI.

Post-irradiation Changes in Peripheral White Blood Cells Observed with Fluorescent Microscopy¹

R HARDING,² A. STEIN, M.D., and J. MAURO, M.D.

KHODAS (1), after subjecting rats to total-body irradiation, observed progressive changes in the white cell counts when the peripheral blood was stained with acridine orange and studied with fluorescent microscopy. Following irradiation, there was a decrease in the number of peripheral leukocytes which fluoresced green and an increase in the number fluorescing yellow, orange, and red. These observations suggested that such changes in circulating white blood cells might serve as an index

copy have been observed following the administration of radiomimetic substances to rats.

It was our purpose to determine whether differential counts on peripheral blood made by fluorescent microscopy could be used as an early sensitive index of irradiation effects in man. It seemed that the peripheral blood might show the changes previously described after total-body irradiation of sufficient intensity. Furthermore, it might be possible to evaluate ex-

TABLE I: DIAGNOSIS AND TREATMENT OF FIFTEEN CASES STUDIED

Case	Sex	Diagnosis	Total Roentgen Dose	Site of Administration
1	F	Anaplastic carcinoma of vagina	2,250	Pelvic
2	F	Duct carcinoma of breast	3,500	Anterior chest
3	F	Squamous carcinoma of cervix	1,255	Pelvic
4	F	Carcinoma of vagina	6,850	Pelvic
5	M	Carcinoma of esophagus	4,200	Anterior chest
6	F	Metastatic carcinoma of breast	1,250	Lumbar spine
7	F	Chronic lymphatic leukemia	925	Splenic
8	F	Multiple myeloma	2,675	Splenic and pelvic
9	F	Carcinoma of cervix	6,760	Pelvic
10	F	Metastatic carcinoma of breast	2,550	Occipital
11	M	Hodgkin's disease	1,800 + mustard	
12	M	Bronchogenic carcinoma	1,470	Anterior chest
13	M	Small-cell malignant tumor in spine	8,150	Head and lumbar spine
14	F	Carcinoma of cervix	2,100	Pelvic
15	F	Carcinoma of cervix	1,800	Pelvic

of the severity of the effect of total-body irradiation. Krasnykh (2), studying bone marrow three, six, and twenty-four hours after total-body low-dose irradiation of rats, also concluded that fluorescent microscopy was valuable in the assessment of early irradiation reaction. These leukocytic alterations were recorded somewhat earlier in bone marrow than were similar changes in peripheral blood. The cytologic changes, however, long antedated classical histologic alterations in bone marrow or other tissues. Similar changes in bone marrow studied with fluorescent micros-

posure in patients who, through industry or accident, received some degree of total-body irradiation.

Graham has developed a group of observations on the normal cells in vaginal smears of patients with uterine cancer after therapy with x-rays which are used as an index of radioresistance or sensitivity of the neoplasm (4). It seemed to us that possibly quantitative differences in the circulating white blood cell counts, determined by fluorescent microscopy, might also serve as an index of radioresistance or sensitivity of the tumor or the host.

¹ From the Department of Pathology, Albany Medical College, Union University, Albany, N. Y. This study was supported by PHS Grant C-5054. Accepted for publication in January 1961.

² National Science Foundation Summer Research Fellow.

MATERIALS AND METHODS

Through the co-operation of our radio-therapist, 15 new ambulatory patients scheduled for therapeutic irradiation were utilized (Table I) for these studies. Blood samples were obtained before treatment and at intervals during the course of therapy. Five hundred cells were counted on each slide, and the numbers of polymorphonuclears with red cytoplasm and mononuclears with red cytoplasm were noted.

Method of Collection: The tip of the third finger was cleansed with alcohol and dried, and a finger puncture was performed, with a sterile hemolet, the blood being drawn by capillary action into a heparinized capillary tube and sealed on the bottom with vinyl putty. The tube was then placed in a microcentrifuge for four minutes, and was then marked with a glass file, approximately 1/16 inch above the buffy coat. The buffy coat and a small amount of red cells were spread out on a clean glass slide, with the end of the capillary tube. The slide was allowed to air dry.

Technic: The details of the staining technic were as follows:

Solutions:

1. *Rehydrator (stock)*
 - (a) Tween "80" . . . 0.5 c.c.
 - (b) Distilled H₂O—qsad 1000 c.c.*Rehydrator (working):* Rehydration time, 5 minutes
 - (a) 1/4 stock (i.e., 60 c.c.) plus
 - (b) 3/4 70 per cent alcohol (i.e., 180 c.c.)
2. *Buffer*
 - $\frac{M}{15}$ Phosphate buffer: to give pH 6.0
 - 1.22 gm. Na₂HPO₄/l
 - 7.9 gm. KH₂PO₄/l
3. *Stain (stock)* (acridine orange, National Aniline Division, Allied Chemical and Dye Corp.)
 - (a) Acridine orange 1.0 gm.
 - (b) Tween "80" 2.0 c.c.
 - (c) Distilled H₂O 1,000 c.c.*Stain (working):* Staining time, 3 minutes
 - (a) Stock stain 100 c.c.
 - (b) Buffer 900 c.c.
4. CaCl₂ anhydrous 0.1M

Staining Procedure:

1. Rehydrator (working) 5 minutes

2. Alcohol 95% 10 minutes
3. Alcohol 80% 5 dips
4. Alcohol 70% 5 dips
5. Alcohol 50% 5 dips
6. Water 5 dips
7. Buffer 3 minutes
8. Stain 3 minutes
9. Buffer 1 minute
10. Differentiate for 30 sec. to 1 min. in CaCl₂
11. Buffer 4 minutes
12. Apply one or two drops of buffer to smeared surface and cover with a cover slip.
13. Remove excess buffer and dry bottom of slide by gently pressing the prepared slide in folds of absorbent cloth (hand towel).
14. Allow one minute for wetting of cells before screening.
15. When screening is completed, remove cover slip.
16. Allow buffer remaining on slide to air dry.
17. Store slides uncovered in slide boxes to avoid slide contact.

NOTE: Destaining may be accomplished by immersing slide in 50 per cent alcohol for ten minutes. Restaining by other methods may then be performed.

It will be necessary to establish the proper time for differentiation in CaCl₂ each time fresh solutions are used. This can only be done *empirically*. One slide should be stained first, mounted in buffer and examined under the microscope. It is properly differentiated if the most immature nuclei present are yellowish-white and show good detail and clear nuclear membranes. It is preferable to start with the shorter time, since if the slides are over-differentiated, they will lose the orange fluorescence.

Equipment: Fluorescence is the emission of longer wave lengths of light from a substance which has been excited by a shorter wave length of light. Intense blue light is used to excite the acridine orange to emit red (RNA) and green (DNA) light.

We have used the Leitz fluorescence outfit with mercury arch UV light source (HB 200), transmission filter BG 12 (8 mm.), and absorption filter OG 1 (2.5 mm.). An American Optical Lamp, 390 B, using the GE H100, A4 mercury vapor lamp is very satisfactory. The transmission filter is a Corning glass filter, 5113 (69 mm.). A Kodak Wratten G (15 G) lacquered filter is used in the microscope above the objective lens or in the oculars as a barrier filter.

Photography: Proper exposure time can be determined only by trial and error, as the usual light meter is not sensitive enough

TABLE II: PERIPHERAL WHITE BLOOD CELL COUNTS DURING RADIOTHERAPY: PERCENTAGE OF MONONUCLEARS WITH RED CYTOPLASM (Fluorescent)

Percentage of Course of Treatment Completed →	0	10	20	30	40	50	60	70	80	90	100
Case											
1	0.40					0.62					1.2
2		0.21						1.4			2.0
3	1.2							7.2			16.0
4			1.2								1.0
5	4.2			2.0		3.8			12.0		20.0
6				1.6							8.6
7	2.1					2.0			1.2		0.60
8			1.7		2.6		3.0	8.0			18.0
9			1.0								1.8
10		1.2									1.8
11		2.2					10.0*				10.0
12	0.80			1.6		4.0					5.0
12		4.2									25.0
14				3.0							3.8
15					1.2						2.1

* After mustard.

to detect the amount of light emitted by the fluorescence. Kodachrome and Anscochrome are satisfactory. Ektachrome film produces an unreal, although brilliant picture. With Kodachrome we have used exposure times of forty-five seconds for magnification $\times 100$ and three minutes for magnification $\times 470$; with Ektachrome, 20 seconds for magnification $\times 100$ and one and a half minutes for magnification $\times 470$.

RESULTS

Fifteen patients were followed, during the course of radiotherapy, by repeated differential counts of peripheral blood with fluorescent microscopy (Table II). It was unusual to see neutrophils with red cytoplasm and, in general, all of the observations were concerned with percentage alterations in the mononuclear cells. It is well known that with radiation there is a lymphocytosis, but these studies indicated a reduction in the percentage of mononuclears with cytoplasm fluorescing green and an increase in percentage of cells with cytoplasm fluorescing red. These alterations became apparent usually after approximately one-half of the treatment course was completed and were without any associated clinical symptoms. The

percentage of mononuclears fluorescing red before treatment varied from 0.4 to 2.1. The highest percentage of mononuclears with red fluorescent cytoplasm was recorded in a patient who received the highest radiation dosage—8,150 r for a rapidly growing, small-cell, malignant tumor, of undetermined primary source. Approximately one-half of the patients showed a marked increase in the number of mononuclears with red fluorescent cytoplasm at the conclusion of therapy. In the remainder, except one, there were insignificant or slight percentage alterations. It is interesting that one patient, who received nitrogen mustard in conjunction with the radiation, showed a very sharp rise in percentage of mononuclears with red fluorescence shortly after the use of the mustard. The only patient who failed to exhibit a percentage alteration had chronic lymphatic leukemia.

DISCUSSION

Increased red fluorescence in the cytoplasm of the mononuclear cells is a semi-quantitative measure of an increased amount of ribonucleic acid. Such increase may be seen in young, actively growing cells or may be the result of direct meta-

bollic disturbance due to radiation. Jaffe *et al.* (5) reported that irradiation of partially hepatectomized rats six or twelve hours after the operation produced a rise in deoxyribonucleoside level in the livers which persisted for about twelve hours.

We feel that the increased RNA in mononuclear cells is a direct effect of irradiation. This finding is duplicated by the administration of nitrogen mustard.

CONCLUSIONS

Progressive alterations in the peripheral white blood cell count after therapeutic radiation in man were observed with fluorescent microscopy. In general, there was a reduction in the percentage of mononuclear cells with cytoplasm fluorescing green and an increase in the percentage with cytoplasm fluorescing red. Although the number of patients in the study is small, it appears that alterations in circulating white blood cell counts observed after acridine orange staining is a sensitive index of

radiation exposure. Approximately one-half of the patients in this small series showed a marked increase in the percentage of mononuclears with red fluorescent cytoplasm. The full implications of these findings must await further clinicopathologic correlation.

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SUMMARY IN INTERLINGUA

Alterationes Post-Irradiatori in le Leucocytyos Peripheric, Observate per Medio de Microscopia Fluorescente

Alterationes progressive in le numeration de leucocytyos peripheric post radiation therapeutic in le homine esseva observate per microscopia fluorescente. In general, esseva notate un reduction in le procentage de cellulas mononucleari con cytoplasma a fluorescentia verde e un augmento in le procentage de tal cellulas con cytoplasma a fluorescentia rubie. Ben que le numero del patientes in le studio es micre, il pare que alterationes in le numeration del circulante

leucocytyos, observate post tincturation a orange acridinic, es un indice sensibile de exposition radiatori. Approximative-mente un medietate del patientes in iste micre serie monstrava un marcate augmento del procentage de mononuclears con cytoplasma a fluorescentia rubie. Le area de signification de iste constationes non pote esser plenemente demarcate ante le obtention de plus extense correlationes clinicopathologic.

Large Screen Image Amplification with Closed-Circuit Television Employing Television Tape-Recorder

BERTRAM R. GIRDANY, M.D., EDWIN S. GAITHER, M.D., and DONALD B. DARLING, M.D.

THE EVER increasing public emphasis on the hazards of radiation and the ever expanding fields of motion radiography present challenges to the radiologist and to the manufacturer of x-ray equipment. At the same time that more extensive use of motion studies is made, every effort must be concentrated on limiting the amount of radiation during any given examination.

The recently opened x-ray department at the Children's Hospital of Pittsburgh utilizes television tape-recording of the fluoroscopic image, mediated through a newly developed image Orthicon television camera² optically coupled to a 9-inch image amplifier. The system permits recording on television tape and simultaneous viewing on the closed-circuit television monitor at the same low levels of radiation as are required for closed-circuit television viewing alone. This paper will outline some of the considerations that went into the planning of the department.

Image amplifiers with field diameters of 4 1/2 and 5 inches have been available for nine years. They have the disadvantages of limited field size and inconvenience of viewing by more than one observer. The optical coupling of Vidicon television cameras with these amplifiers to record the fluoroscopic image on closed-circuit television monitors solved the problem of viewing but necessitated increased amounts of radiation for adequate visualization of the field under observation. Satisfactory cineradiographic film recording of the fluoroscopic image on the amplifier requires a major increase in radiation.

In the course of investigation of available systems of image amplification, particularly with reference to larger field size,

the authors became interested in the General Electric TVX system, which employed closed-circuit television as an integral part of its operation. It offered the potential advantage of television viewing at diminished rates of radiation but raised the problem of recording the television image. Kinescopic movie-film recording of the image on the television screen is relatively difficult technically, moderately expensive, and attended by film problems inherent in other cineradiographic methods. Television tape-recording affords the ideal method for reproduction of the picture on the television monitor. The identity of an original picture with its television-taped reproduction is apparent to any home television viewer. Television tape also offers the advantages of immediate playback for review, and of availability to all fluoroscopic rooms. An additional cable run from the television camera to the tape-recorder allows recording from each fluoroscopic unit. Television tape-recording is possible at the level of radiation required for closed-circuit television monitor viewing.

The TVX equipment available three years ago was not suitable for routine work in a pediatric x-ray department, but the interest in television tape-recording carried over to the exploration of its use with other methods of image amplification. Closed-circuit television monitoring, as noted, has been available since the advent of image amplifiers; the accepted method optically coupled a Vidicon camera with the image phosphor on the image amplifier. Acceptable pictures required as much, or more, radiation than full-screen standard fluoroscopic examinations. The efficiency

¹ From the Department of Radiology, Children's Hospital of Pittsburgh, and the University of Pittsburgh, School of Medicine, Pittsburgh, Penna. Presented as a Work in Progress report at the Forty-sixth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 4-9, 1960.

² Televex by Westinghouse Electric Corporation.

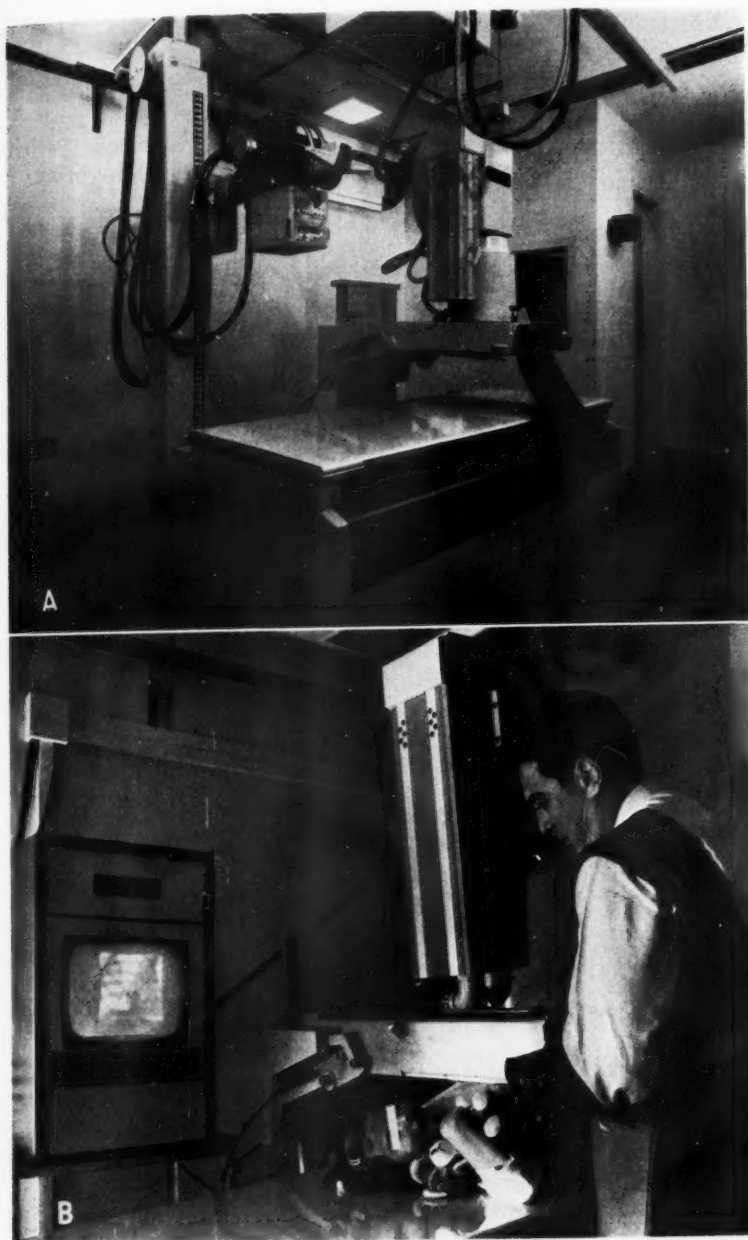


Fig. 1. A. An x-ray fluoroscopic room at the Children's Hospital of Pittsburgh containing the Teleflex unit.

B. Photograph made during actual fluoroscopic visualization of the chest. The major circuitry is housed in the monitor.

of optical coupling of the Vidicon camera to the image phosphor was 10 per cent, with a 90 per cent light loss.

It should be possible to combine a Vidicon camera directly with the image amplifier in the same glass envelope and

thereby eliminate light loss. This arrangement, however, would not be practical; such coupling would be permanent and would ignore the fact that image amplifiers are not predictably uniform in their manufacture and must be checked for efficiency and amplification before use. Moreover, breakdown of the Vidicon

of closed-circuit television viewing of the fluoroscopic image. The image Orthicon tube should allow television viewing of the fluoroscopic picture at levels of radiation similar to or below that employed in standard image amplification. It seemed reasonable that the complicated circuitry of the image Orthicon camera might be

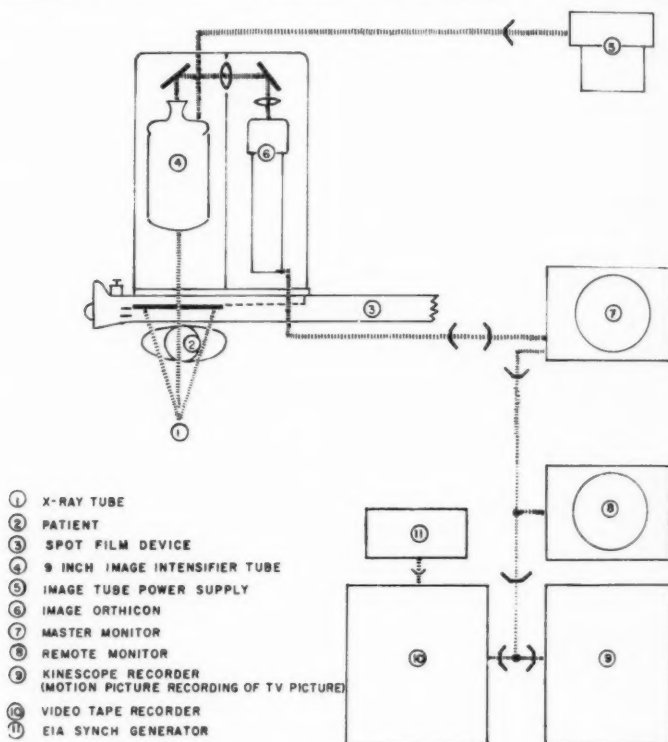


Fig. 2. Schematic diagram of the television and tape-recording system. Westinghouse Televex.

circuitry might necessitate scrapping of the entire combination of amplifier-Vidicon system.

Image Orthicon television cameras are approximately a thousand times more sensitive to light than standard Vidicon cameras. In other respects the systems are essentially similar save that the Orthicon circuitry is more complicated, and the image Orthicon camera is more expensive.

The optical coupling of an image Orthicon camera with a large-field image amplifier would seem to offer an ideal method

placed remotely with respect to the image amplifier, so that the bulk of the combined amplifier and camera would not be a factor in the practical application of this coupling. This proved possible (Fig. 1).

In the course of the development by Westinghouse of the specially designed image Orthicon camera for fluoroscopic use, an attempt was made to link the camera with a light intensifier. This was based on the availability of a camera specifically employed for night aerial photography. The light intensifier was to pick up directly light from a standard

Patterson B-2 fluoroscopic screen, and deliver the intensified image to the camera. This attempt was unsuccessful and demonstrated the basic problems in use of light amplification. The law of inverse squares explained the excessive loss of light from the fluoroscopic screen because the wide angle $f.9$ lens had to be removed a suf-

ated through electronic methods employed in currently available image amplifiers.

Figure 2 is a diagrammatic representation of the closed-circuit television fluoroscopic system developed by Westinghouse for the Children's Hospital of Pittsburgh and currently in use there. As part of this system there is an electronic magnifier



Fig. 3. The RCA television tape-recorder.

ficient distance to allow optical coverage of the entire screen. There was also loss of light through the lens. At these low levels of light intensity the behavior of the image Orthicon tube was erratic and the predicted gain through the image Orthicon system was not achieved.

It would seem from these observations that any system depending on intensification of the actual light from the fluoroscopic screen will prove unsatisfactory; such systems will probably be better medi-

that doubles the size of the television image when small areas are being observed. By effectively scanning with twice the number of lines, the magnifier enhances detail in small areas. Four fluoroscopic rooms are connected by co-axial cables to the television tape-recorder (Fig. 3). Remote monitors are installed in the chief radiologist's office and the x-ray reading room.

Convenience of viewing and improved teaching are the major advantages of

closed-circuit television observation of fluoroscopic images. Simultaneous viewing by an unlimited number of observers is practical. Supervision of trainees by senior radiologists is feasible.

The addition of television tape-recording amplifies the basic advantages described. Tape-recording of the television image is carried out at the same low levels of radiation as are employed for closed-circuit television monitoring. In the x-ray department of the Children's Hospital of Pittsburgh, satisfactory television viewing and recording are obtained with settings ranging from 0.13 to 0.5 ma and 60 to 80 kv. The examinations varied from the chests of small infants to gastrointestinal series in teen-aged adolescents.

The television tape can be played back immediately for re-evaluation by the radiologist or in consultation with other members of the hospital staff. The tape may be stored, or it can be transferred, *via* a cine-recording camera, to fine-grain movie film. This latter step is necessary for single frame or slow motion viewing, since neither of these is currently possible with television tape.

The advantages of television tape-recording become more apparent with increasing use. A prime consideration is reduction in radiation to patients through avoidance of re-examination at time of consultation. All fluoroscopic examinations are readily recorded and may be reviewed at leisure an unlimited number of times, without re-exposing the patient to radiation. The recording on the tape is erased when the tape is used to record other examinations. The saving in time of hospital personnel is great. The dozen or more people involved in re-examining a patient are not called into action; rather, the taped examination is reviewed.

The resident in radiology can be more easily supervised and his examinations reviewed with him without the cost in patient radiation or in time of hospital personnel. A library of fluoroscopic examinations can be as available as still "teaching file" films.

Controversial and puzzling problems can be reviewed at times convenient for consultants. The actual fluoroscopic record rather than the spot-films will be available, although films can be made during fluoroscopy.

It has become clear to us, in a relatively short period of use, that the fluoroscopic examiner, who has many things to contend with besides observing the fluoroscopic image, misses much of what he sees. He observes infinitely more when he reviews a taped recording of his examination, at which time all of his resources can be concentrated on the viewing process.

Motion studies of opaque material, as in angiography, allow simultaneous viewing during the recording process, so that the technical quality of the examination is certain; the examiner can be assured that what he wants to visualize has been demonstrated. Immediate playback allows him to check his impressions in this respect. The low levels of radiation needed for recording allow prolonged, or repeated, examinations without radiation hazards becoming a limiting factor.

The availability of sound recording on the television tape offers a new and largely unexplored field for simultaneous studies of motion radiography with sound. There is immediate application in the understanding of speech and cleft palate problems.

CONCLUSION

The authors have described some of their experiences with closed-circuit television viewing of the fluoroscopic image and with closed-circuit television tape-recording. Much remains to be learned in this ever expanding and exciting field.

ACKNOWLEDGMENTS: The authors are indebted to the X-ray Division of the Westinghouse Electric Corporation, and to Messrs. W. P. Lamons and John Ross in particular, for their help and cooperation in the developments described. Mr. W. I. McCord of the Radio Corporation of America rendered invaluable assistance in the installation of the television tape-recorder.

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SUMMARIO IN INTERLINGUA

Amplification de Imagine a Grande Ecran, con Television a Circuito Claudite, Utilisante un Registrator a Banda Televisional

Le autores describe certas de lor experientias in le presentation, per television a circuito claudite, de imagines fluoroscopic e in le registration a banda pro television a circuito claudite, a base del disveloppamento de iste methodos al Hospital pro Juveniles a Pittsburgh. Le systema fluoroscopic de television a circuito claudite include un magnificator electronic que duplica le dimensiones del imagine de television quando restringite areas es prendite sub observation. Per duplicar le numero del lineas de exploration, le magnificator promove le claritate del detalios in tal restringite areas. Quattrosal as fluoroscopic es connectite per cabo co-axial con le registrator a banda televisional, e distante stationes monitori es installate in le bureau del radiologo in chef e in le sala de lectura roentgenologic. Observation si-

multanee per un numero illimitate de personas es practicabile, e le surveillantia de practicantes per radiologos experte pote esser arrangiate.

Le registration a banda es effectuate ab le imagine televisional al mesme nivellos de radiation que es empleate in le television a circuito claudite. Resultatos satisfacente in le television e in le registration es obtenite con adjustmentes de inter 0,13 e 0,5 milliampere e de inter 60 e 80 kilovolt.

Un major avantage del registration a banda es le reduction del radiation recipite per le pacientes, gratias al possibilitate de ommitter repetite examines. Le registration pote esser re-vidite a non importa qual tempore, sin re-exponer le patiente. Le economia de tempore pro le personal del hospital es etiam un avantage.



Apparatus and Technic for the Administration of Intracavitary Radioactive Isotopes¹

NORMAND J. MICHAUD, B.S., and LEONARD M. LIEGNER, M.D.

THE METHOD of administration of radioactive isotopes in the treatment of pleural effusions and ascites associated with cancer will vary according to the therapeutic technic (1-5). A procedure with a suitable apparatus that utilizes an economical and sterile disposable package is described in this paper.

loidial chromic phosphate (P^{32}) or colloidal gold (Au^{198}), can be obtained in the exact amount prescribed.

The entire apparatus is assembled within a few minutes under sterile conditions (Fig. 2). Before the hypodermic needles are inserted into the radioactive isotope vial, the air is removed from the tubing

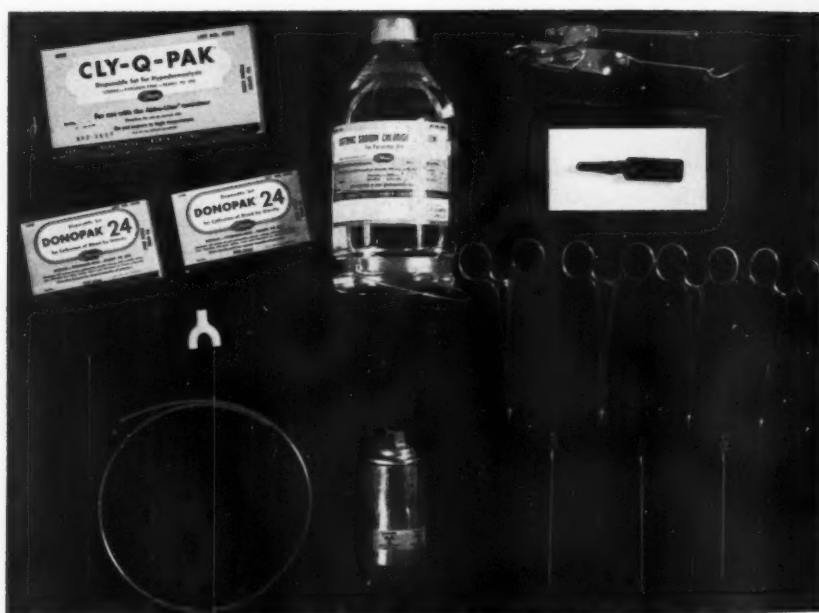


Fig. 1. Apparatus for radioactive isotope administration.

The apparatus, shown in Figure 1, consists of: polyethylene or nylon tubing with an interior diameter of 0.70 inch; 4 stainless steel clamps; 3 No. 15 hypodermic needles of 3 1/2 inches length; 1 ampule of 5.0 c.c. Evans blue; 500 c.c. isotonic saline solution; 1 Cly-Q-Pak²; 2 Donopak 24²; one Y connector.² All the equipment is supplied sterile or can be sterilized.

The radioactive isotope, whether col-

by the flow of saline in each segment. Each section is then clamped.

The shielded radioactive isotope is then placed on a table or stand and the rubber seal of the vial is swabbed with alcohol or iodine. The inflow needle is inserted just through the rubber stopper and the outflow needle is inserted to the bottom of the vial. This procedure is carried out without removing the vial from the lead container (Fig. 2).

¹ From the Radiation Therapy Department, St. Luke's Hospital, New York, N. Y. Accepted for publication in January 1961.

² Abbott Laboratories, North Chicago, Ill.

If the radioactive isotope is a colorless liquid, then 0.5 c.c. of Evans blue can be injected with a syringe into the gum rubber tubing attached to the inflow needle entering the isotope vial. The final act is to insert the needle at "C" (Fig. 2) into the polyethylene or nylon tubing protruding from the patient.

As the patient is presumed to have had a successful paracentesis or thoracentesis, clamps 1 and 2 (Fig. 2) are unfastened so that saline only will flow into the body cavity. Any amount of saline can be administered prior to the flow of the radioactive isotope. Clamp 2 is then fastened to its original position and clamps 3 and 4 are unfastened. The saline solution will flow and pick up the Evans blue and the radioactive isotope. It is now possible to see the blue isotope liquid flow into the patient in a matter of a few minutes. As the flow of saline continues through the system the liquid will become colorless, thus indicating that all the isotope has entered the patient.

To drain the system, all clamps as well as the bottle of saline solution are removed, and the saline bottle cap with tubing attached is held sufficiently high so that all the liquid flows from the system. When all the liquid has drained into the patient, the segment of tubing between "A" and the saline bottle cap is clamped off. As the physician begins to tighten the purse-string suture placed around the paracentesis site an assistant carefully removes the polyethylene catheter from the patient and delivers the tip into a gauze pad; simultaneously the purse suture is tied. The paracentesis site is then dressed.

The entire unit, minus the clamps, is placed in a paper or plastic bag and stored for later disposal. All personnel who participate in the administration wear rubber gloves and are monitored for contamination before discarding gloves or equipment.

For a satisfactory tap, the preparation of the paracentesis site is made before the assembly of the apparatus. A successful paracentesis insures the location of the cavity. Upon removal of the paracen-

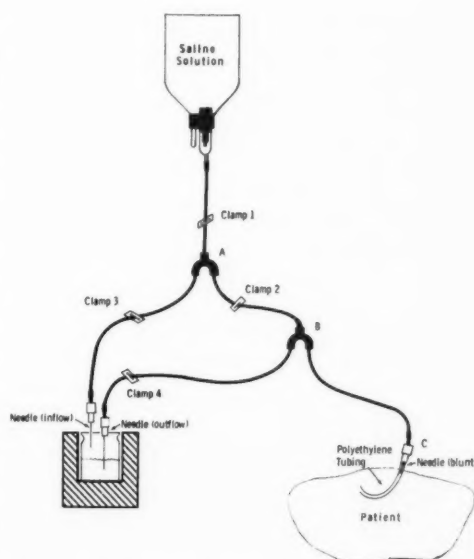


Fig. 2. Schematic diagram of apparatus for the administration of the radioactive isotope solution.

tesis trocar, the polyethylene or nylon tubing shown (Fig. 1) is threaded through the hollow cannula into the peritoneal cavity with a 5-inch length protruding from the patient. A purse-string suture is placed about the paracentesis site. The cannula is then withdrawn, leaving only the catheter in place. This is removed when the isotope has been administered as described above.

For intrapleural administration a successful thoracentesis will insure the location of the cavity. A Kelly forceps is clamped to the aspiration needle near the skin surface to maintain the needle's position. After the pleural cavity is entered and fluid flow assured, a 3-way stopcock, which is used to ensure a closed system, is adjusted so as to direct the flow into a vacuumized collection bottle. The aspirating syringe can be conveniently removed. When sufficient fluid has been withdrawn from the pleural cavity (a complete tap is not desirable), the connection at "C" (Fig. 2), without needle attached, is inserted into the 3-way stopcock position formerly occupied by the aspiration syringe. The stopcock is then

adjusted so that the isotope system is continuous with the pleural cavity. Saline is then allowed to flow through the bypass designated "A" "B" "C" (Fig. 2), to confirm proper flow. Thereupon the steps described above for administration of the isotope are carried out.

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SUMMARIO IN INTERLINGUA

Apparato e Technica pro le Administration Intracavitari de Isotopos Radio-Active

Es describe un technica pro le administration de isotopos radio-active post paracentese in le tractamento de maligne effusiones pleural o ascites. Illo require le uso de duo agulias hypodermic que es inserite in le flasco de isotope, 500 cm³ de isotonic solution salin, un pecia de tubage polyethylenic con appropriate crampas pro regular le fluxo del solution salin o isotopic, un ampulla de blau de Evans, un connexion in forma de Y, un "Cly-O-Pak" e 12 "Donopaks."

Le solution salin es primo inviate a transverso le tubage pro liberar lo de aere. Postea illo accepta le isotope (que es col-

orate pro le blau de Evans), e isto es facite fluere ad in le cavitate peritonee o thoracic via le sito del paracentese. Durante que le fluxo continua, le liquido deveni incolor, indicante que omne le isotope ha entrate in le patiente.

Post le completion del administration del isotope, le complete apparatura—con le exception del crampas—es placiata in un sacco de papiro o plastic pro esser abducite plus tarde. Omne le personal participante in le administration porta guantos de cauchu e es scrutinate pro contamination ante que le guantos o le equipamento es discartate.

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Death Following Intravenous

Carbon Dioxide Angiocardiography¹

HARVEY I. MEYERS, M.D., and GEORGE JACOBSON, M.D.

THE FIRST KNOWN death following the intravenous injection of carbon dioxide to outline the right atrial wall and adjoining structures roentgenographically is here reported. The method used was that suggested by Paul, Durant, Oppenheimer, and Stauffer (1, 2) and consists briefly of injecting 50 to 100 c.c. of pure CO₂ into the tubing of an intravenous infusion with the patient in the left lateral decubitus position. Roentgenograms are made after the injection, with a horizontal x-ray beam. With the patient in this position, the CO₂ collects in the right atrium. The combined thickness of the endocardium, myocardium, pericardium, and pleura, together with their respective spaces, is outlined in the resulting roentgenograms. The procedure has been used mainly for detecting pericardial effusion.

Up to the time of the examination to be described here, no fatalities had been reported as a result of this technic. Dr. Herbert Stauffer (3), who has performed a large number of these examinations, is unaware of any previous deaths.

CASE REPORT

A 48-year-old Negro female was admitted to the Los Angeles County Hospital because of swelling of the feet, with gradual extension up the legs and shortness of breath. One of the possible clinical diagnoses was pericarditis with pericardial effusion. Roentgenograms demonstrated extensive infiltration in both lungs, several cavities in the right upper lobe, and a moderately enlarged heart. A chest film made a year before in another hospital was reported to be negative.

The patient was critically ill, and angiocardiography was undertaken to determine whether or not pericardial effusion was present. In the left lateral decubitus position, 100 c.c. of CO₂ was injected in the antecubital vein through an intravenous infusion tube. Several films were exposed. Approximately three minutes after the completion of the injection, the technician noted that the patient was

unresponsive. Artificial respiration and oxygen under bag pressure were given immediately. Since no heart beat was audible and no spontaneous respirations were detectable, the chest was opened and cardiac massage was instituted. Spontaneous heart beat was restored after two episodes of fibrillation, which were corrected by electrical defibrillation. The chest was closed and the patient was placed in hypothermia, with an intravenous neosynephrine drip to maintain the blood pressure. Despite this, death occurred four hours after the onset of cardiac arrest. An autopsy was not permitted.

COMMENT

The exact cause of death in this case is unexplained. The high degree of safety of the procedure has been pointed out by Stauffer *et al.* (1) and Scatliff *et al.* (4). It is difficult to attribute death to the amount of CO₂ injected since, as has been pointed out by the last-mentioned authors, "50 to 100 c.c. alter the carbon-dioxide content of the blood approximately 5 to 10 volumes per cent, and this effect is of only several minutes duration. In this time the change produced in the blood pH is insignificant. This amount of carbon dioxide is equivalent to the amount of the gas formed in one minute during minimal exercise, such as eating or turning over in bed." While this patient did have considerable lung disease, her serum bicarbonate level was 22 mEq/liter (N=24-29) and at this level one would not expect such susceptibility to the amount of CO₂ injected intravenously.

Gas embolism, another theoretical possibility, also seems unlikely in this case. Carbon dioxide is twenty times more soluble in blood than oxygen or air and therefore dissolves rapidly. The left lateral decubitus position is utilized to keep the CO₂ trapped in the right atrium until this occurs. In the present case the patient was maintained in the

¹From the Radiology Department of the Los Angeles County General Hospital and the University of Southern California School of Medicine, Los Angeles, Calif. Accepted for publication in February 1961.

left lateral decubitus position until resuscitation measures were instituted. The third film, taken two and a half minutes after gas injection, showed that most of the CO₂ had already been absorbed from the right atrium.

A third possibility is that nitrogen may have diffused into the CO₂ bubble, as has been shown to occur experimentally by Scatliff. This also appears to be an unlikely factor in this case since so little gas remained in the atrium less than three minutes after injection.

SUMMARY

A death following intravenous CO₂ angiocardiology in a patient with extensive lung disease is reported. This

is the first known fatality from this procedure. The mechanism of death was not established.

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Los Angeles 33, Calif.

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SUMMARIO IN INTERLINGUA

Morte post Angiocardigraphia a Intravenose Bioxydo de Carbon

Le injection intravenose de bioxydo de carbon pro angiocardigraphia ha essite considerate como distinguite per un alte grado de securitate. Le hic-reportate caso, secundo le informationes del autores, es le prime in le litteratura in que le manovra esseva sequite de morte.

Le patiente esseva un feminina negre de quaranta-octo annos de etate con extense morbo pulmonar e un possibile effusion pericardial. Con le patiente in decubito

sinistro-lateral, 100 cm³ del gas esseva injicite in le vena antecubital. Le action del corde cessava circa tres minutas post le completion del injection. Le thorace esseva aperite, e massage cardiac resultava in un restauration temporari del action cardiac, sed morte superveniva intra quatro horas. Un necropsia non esseva effectuate, e—per consequente il non esseva possibile establir le mecanismo del morte.

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EDITORIAL

Roentgenology in the Teaching Hospital

With the increasing size of major hospitals, the problem of organization of work confronting the staff radiologist is becoming more complex. In the teaching hospital, his difficulties are compounded. Direct comparison between major teaching hospitals and their component departments in different areas of the world is both difficult and invidious. Such hospitals, however, cannot long afford to ignore what appear to be promising or soundly established methods employed in other medical centers.

Major departments of radiology the world over are beset by a common problem—limited opportunities for expansion to meet both the steadily growing demand for long established technical procedures and the ever rising tide of newer and more complex radiological examinations.

In Great Britain, where the National Health Service has provided ready access to statistical information regarding the growing utilization of the more specialized diagnostic radiological procedures over the ten years from 1951 to 1959, the time required of consultant radiologists to handle these procedures increased by 50 per cent during this period, in the average teaching hospital. This does not include the additional time spent by junior staff radiologists in conducting or supervising these examinations. It is, therefore, hardly surprising that one finds a widespread interest in the planning and organization of radiological departments.

The difficulty in maintaining increases in radiological staff commensurate with the increasing demands is almost universal. Under these circumstances (which have become well established facts of life), some aspects of the practice of radiology must inevitably suffer. This is the universal

theme, even in the best of departments. The variations on it are numerous and depend upon local circumstances.

Major factors determining what aspects of the work of a radiology department will flourish include, first, the number of staff radiologists, their personalities, and their fields of particular interest. In this connection, radiological residents have a great opportunity to modify the character of a department for the better.

Where the size of the staff and the available facilities fall short of the optimum requirements, the relative aggressiveness or complacency of the clinical staff in different specialties may determine in what direction or directions the major effort will be made and even the direction of the growth of the department.

Finally, of course, the hospital administration has a great responsibility, since the business acumen of this group must determine what funds become available for expansion and its wisdom will determine their distribution. It seems that the success or failure of any proposal to expand radiological facilities, the direction of expansion, the type of equipment chosen, the priorities given to the use of space and equipment and the like, depend principally upon the foregoing factors and their interaction. Parenthetically, it is probable that few businesses would long survive such scanty investment of their profits for further growth as the majority of radiological departments usually suffer.

It seems generally true that, within the framework of existing circumstances, some of the responsibilities which should be borne by a radiological department are sacrificed, either deliberately and with sad acceptance, or by insufficient attention and effort, leading to a failure to thrive. In

this connection, it is interesting to observe that, in the course of time, as members of the radiological staff come and go, so will different segments of the radiological work come to flower or wither, according to the energies, personalities, and special interests of the individuals.

What standard are we striving to reach and to maintain? This is difficult to define adequately. Obviously, perfection in radiological diagnosis and radiation therapy is impossible of attainment. Perhaps we could oversimplify by saying that the minimum desirable standard in any given facet of radiological activity, including research, is that degree of excellence which is regularly exhibited in those institutions primarily dedicated to that field of medical endeavor. Also, we should regard it as important that this standard be achieved promptly and principally as a result of the spontaneous efforts of radiologists, rather than belatedly and largely due to pressure from our clinical colleagues. It might be pertinent to stress here the importance of the radiologist seeing and digesting more radiological material in a given sphere of radiological practice than any single clinical colleague. It is desirable also that he find sufficient time to keep fully abreast of advances in that area of medical practice. This should include reasonable time to attend special rounds of the clinical staff, so that he may early become aware of clinical problems and take his rightful place in the search for solutions.

Thus stated, the magnitude of the problem is readily apparent and it is not surprising that radiological departments of busy, general hospitals, even of the first magnitude, fall short of the ideal in at least some respects. Indeed, it would require that almost unlimited staff, funds, and space be available before any close approach to the ideal could be achieved. In practice, therefore, our problem becomes one of search for the best possible compromise.

In many areas, radiology has become so sophisticated, the literature so extensive,

and advances so rapid that no ordinary radiologist can keep pace and occasionally take the lead, if his energies and time are greatly diluted by the necessity for giving equal attention to, and accepting equal responsibility in, all of the many aspects of radiological practice in a given department. Should we then advocate that he take training in one specialized branch of radiology (such as the neurological, cardiovascular, urological, or gastrointestinal) and devote his career in a teaching hospital department exclusively to that subspecialty?

This would again be most undesirable, since one of the fascinations and, indeed, strengths of the practice of radiology is the wide diversity of the fields into which it can take us. Also, it is a practical necessity in a busy general hospital that one radiologist be able to take over the responsibilities of another, to cover the exigencies of leave, change of staff, and illness. On the other hand, it is generally true that the best diagnostic results and major advances in technic are favored where radiologists regularly undertake full responsibility for specialized diagnostic examinations, including "minor" surgical procedures, such as are required in cerebral and peripheral angiography, aortography, encephalography, and the like. In North America, economic factors, pressure of time, and perpetuation of combined training in and practice of diagnostic and therapeutic radiology make such an undertaking difficult. There has, however, been a gradual trend in this direction during the past decade. This is due at least partly to the influence of Europe, where in many countries it is the rule rather than the exception for such procedures to be the responsibility of the radiologist. Advantages of this method of practice include: better control of the radiographic technic, as related to the surgical technic employed, and of the technical requirements for a suitable radiographic result; avoidance of the difficult position of the radiographic technician under orders from someone unfamiliar with radiographic problems to work contrary to sound practice. Even under

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the best circumstances, it is undesirable that procedures performed in a department of radiology be under the control of members of another department, or of a visiting physician or surgeon. In such circumstances it is more difficult for the radiologist to maintain his rightful place in the medical community.

In established departments that have been forced to grow in an irregular ameboid fashion over many years, really radical changes in the overall design of the physical facilities are obviously too costly to be practical. Certain principles of organization may still be applied, however, and should go some way toward developing the maximum potential of both the staff and the radiological facilities.

There is much to be said in favor of the practice in some large Scandinavian hospitals of daily display of all radiographs of current clinical problems. These remain on view for combined ward rounds and teaching, with a saving of much time usually lost in the repeated handling of films in envelopes. This plan, however, generally demands a large amount of space, already at a premium. The slide magazine viewing illuminator, originally designed for handling the numerous radiographs obtained in neurologic examinations, can help offset the problem of space. By this means, the viewing space required for a large number of radiographs may be reduced to as little as one-twelfth of that needed when conventional illuminators are used.

Clerical staff may be trained to set up and take down the bulk of the day's work on such illuminators, thus saving the radiologist considerable time in sorting and handling films, particularly in the case of chronic clinical problems, neurologic and serial cardiovascular examinations, and conditions of unusual interest. The improved opportunities for teaching are obvious.

With many conflicting needs in mind, the following broad plan might serve as a basis for developing the best compromise in any given large general teaching hospital.

Let us first consider the different areas of medical practice that are not infrequently segregated into specialized institutions—such as neurological institutes, eye and ear infirmaries, children's hospitals, etc. Can we design radiological diagnostic units specifically for each of these special fields, equipping and staffing each in such a way that it is largely self-sufficient, and then attempt to integrate these units so that they become parts of a large department of a general hospital? In the process of integration, one would attempt to sacrifice as little as possible in each unit, but throughout would keep in mind the good of the whole.

Where new construction is contemplated, the individual diagnostic units might conveniently be grouped in a radial or H arrangement, or some modification of such. It would probably be convenient to have interpretation areas, including magazine viewing illuminators, near the entrance of each unit from the main connecting corridor or plaza, so that all the interpretation and film demonstration areas would be as close to one another as possible. This would facilitate free consultation between members of the staff.

The size of each unit would naturally be proportional to the expected patient volume in that particular field in the given institution and the equipment would be selected specifically for the work involved and with regard to the special procedures commonly to be undertaken in the unit. Specialized equipment can also be used very effectively for many routine studies. In some cases, a little ingenuity will suggest an inexpensive modification which will greatly extend the potential uses of such equipment. This is particularly important in the plan envisaged here since, during peak patient loads in one unit, overlapping into less busy units would be employed to spread and equalize the strain.

Central filing is of paramount importance. Nursing, technical, and secretarial staff could be organized on a central basis, but there would be a need for a senior technician in each unit, responsible for

routine radiography and training in that unit only. Other radiographers, including students, could rotate between units at intervals of one or more months.

A staff radiologist with suitable special postgraduate training would be responsible for each unit, under the chief radiologist, and would be assisted by one or more radiologists where necessary. Residents would rotate through the units during the training period. It would be anticipated that the radiologists and residents would spend part of each day attending other units in turn. A daily radiological round of all units, for discussion of the most interesting problems of the day, should be possible. In this connection, every effort

to defy Parkinson's law that "work expands to fill the time available for its completion," would be necessary!

This country is being called upon to prove, in every sphere of activity, that private enterprise can compete successfully with other, less flexible forms of social organization. This heavy responsibility demands constant vigilance, no less in the matter of methods of medical practice than in political and economic spheres, lest power be lent to the arguments of those who seek to persuade that greater efficiency is offered by systems embodying control by the state.

PAUL F. J. NEW, M.B.,
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ANNOUNCEMENTS AND BOOK REVIEWS

ALABAMA RADIOLOGICAL SOCIETY

Recently elected officers of the Alabama Radiological Society are: Samuel F. Crabtree, M.D., Anniston, President; Richard D. Glasgow, M.D., Fairfield, Vice-President; Walter J. Brower, M.D., 2001 11th Ave., S., Birmingham, Secretary-Treasurer.

BUFFALO RADIOLOGICAL SOCIETY

At the May meeting of the Buffalo Radiological Society the following members were elected to office: Sawyer A. Glidden, M.D., President; Kenneth H. Seagrave, M.D., Vice-President; R. Joseph Naples, M.D., 106 Morgan Parkway, Williamsville 21, Secretary; Edward A. Dunlap, Jr., M.D., Treasurer.

EASTERN RADIOLOGICAL SOCIETY

At the April meeting of the Eastern Radiological Society officers were elected as follows: Robert E. Wise, M.D., Boston, Mass., President; Norman Heilbrun, M.D., Buffalo, N. Y., Vice-President; James F. Martin, M.D., 300 S. Hawthorne Rd., Winston-Salem 7, N. C., Secretary-Treasurer; and Mortimer Lubert, M.D., Shaker Heights, Ohio, Chairman Scientific Sessions.

FLORIDA RADIOLOGICAL ASSOCIATION

Recently elected to office in the Florida Radiological Association, for the year 1961-62, are: John P. Ferrell, M.D., St. Petersburg, President; Alfred G. Levin, M.D., Miami, President-Elect; Ivan Isaacs, M.D., Jacksonville, Vice-President; Richard D. Shapiro, M.D., 1680 Meridian Ave., Miami Beach, Secretary; Marvin V. McCloy, M.D., Jacksonville, Treasurer.

MEMPHIS ROENTGEN RAY SOCIETY

At a recent meeting of the Memphis Roentgen Ray Society the following officers were elected: Boyer M. Brady, Jr., M.D., President; Marvin M. Keirns, M.D., Vice-President; Irving K. Ettman, M.D., Department of Radiology, Kennedy VA Hospital, Memphis 15, Tenn., Secretary.

The Society meets the first Monday of each month at John Gaston Hospital.

MILWAUKEE ROENTGEN RAY SOCIETY

During 1961-63 the officers of the Milwaukee Roentgen Ray Society will be: Gene W. Sengpiel, M.D., President; Joseph F. Wepfer, M.D., Vice-President; Abraham Marck, M.D., 2500 N. 108th St., Milwaukee, Secretary-Treasurer.

NASSAU RADIOLOGICAL SOCIETY

The Nassau Radiological Society (New York) has elected the following officers for the coming year: Seymour Wasserman, M.D., Bay Shore, President; Alan Baum, M.D., Hicksville, Vice-President; Robert Tugendhaft, M.D., Meadowbrook Hospital, Hempstead, Secretary; Harold Chiat, M.D., Garden City, Treasurer.

The Society meets on the second Tuesday of the month in February, April, June, October, and December.

RADIOLOGICAL SOCIETY OF NEW JERSEY

In May 1961 the Radiological Society of New Jersey elected its officers for the ensuing year: W. Laurence Bonnet, M.D., Trenton, President; Jules H. Bromberg, M.D., Newark, Vice-President; Harry J. Perlberg, Jr., M.D., Jersey City, Treasurer; George H. Burke, Jr., M.D., 601 Grand Ave., Asbury Park, Secretary.

RADIOLOGICAL SOCIETY OF THE STATE OF NEW YORK

The following are the new officers of the Radiological Society of the State of New York: Frank J. Borrelli, M.D., New York, President; Norman Heilbrun, M.D., Buffalo, Vice-President; John W. Colgan, M.D., 273 Hollywood Ave., Rochester 18, Secretary-Treasurer.

OKLAHOMA STATE RADIOLOGICAL SOCIETY

Newly elected officers of the Oklahoma State Radiological Society are: E. D. Greenberger, M.D., McAlester, President; G. Ray Ridings, M.D., Oklahoma City, Vice-President; Simon Pollack, M.D., Utica Square Medical Center, Tulsa, Secretary; Gene Coin, M.D., Oklahoma City, Treasurer.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY

The Pacific Northwest Radiological Society held its 15th annual meeting May 13 and 14, at the Benson Hotel in Portland, Ore. Dr. Homer Hartzell of Seattle, Wash., was installed as the new President of the Society, and the following were elected to office: John A. Ireland, M.D., Vancouver, B.C., President-Elect; H. M. Edmison, M.D., Victoria, B. C., First Vice-President; M. Marvin Wallace, M.D., Seattle, Wash., Second Vice-President; John N. Burkey, M.D., 509 Olive Way, Seattle, Wash., Secretary-Treasurer. J. W. Loomis, M.D., Portland, Ore., was elected to the Executive Committee for a three-year term.

The organization will hold its 1962 convention in Seattle, Wash.

PENNSYLVANIA RADIOLOGICAL SOCIETY

At the annual meeting of the Pennsylvania Radiological Society held in May 1961, the following officers were elected: Robert P. Barden, M.D., Philadelphia, President; Walter P. Bitner, M.D., Harrisburg, President-Elect; John W. Hurst, M.D., Altoona, First Vice-President; Erwin Beck, M.D., Pittsburgh, Second Vice-President; Frederick R. Gilmore, M.D., Clearfield Hospital, Clearfield, Secretary-Treasurer; John H. Harris, Jr., M.D., Carlisle, Editor; Marlyn W. Miller, M.D., Altoona, Associate Editor; John H. Harris, Sr., M.D., Harrisburg, Councilor to American College of Radiology; Newton Hornick, M.D., Pittsburgh, Alternate Councilor to American College of Radiology.

The next annual meeting will be held at Pocono Manor Inn on May 25-26, 1962.

SOUTH CAROLINA RADIOLOGICAL SOCIETY

The South Carolina Radiological Society recently elected as officers for the coming year: President, J. Harvey Atwill, Jr., M.D., Orangeburg; Vice-President, L. Haynes Barr, M.D., Sumter; Secretary-Treasurer, George W. Brunson, M.D., 1406 Gregg St., Columbia; Councilor to the American College of Radiology (hold over), George W. Smith, Jr., M.D., Columbia; Alternate Councilor to the American College of Radiology, William P. Tinkler, M.D., Greenwood.

TENNESSEE RADIOLOGICAL SOCIETY

New officers of the Tennessee Radiological Society are: President (1961): Edward H. Mabry, M.D., Memphis; President-Elect, M.D. Ingram, Jr., M.D., Nashville; Vice-President, James J. Range, M.D., Johnson City; Secretary-Treasurer, B. M. Brady, Jr., M.D., St. Joseph Hospital, Memphis. Walter E. Scribner, M.D., of Kingsport was nominated Councilor to the American College of Radiology.

SOCIEDAD PERUANA DE RADIOLOGIA

At a recent meeting, the Sociedad peruana de radiologia elected the following officers for 1961-1962: Dr. Amador Holgado Valer, President; Dr. Enrique Gonzales Vera, Vice-President; Dr. Germán Sanchez Checa Ch., Secretary-General; Dr. Fernando Robinzon, Secretary of the Proceedings; Dr. Wenceslao Posell Pinillos, Treasurer; Dr. Jorge de la Flor Valle, Secretary of Scientific Activities. The address of the Society is Apartado 2306, Lima, Peru.

CONTINUATION COURSE UNIVERSITY OF MINNESOTA

A continuation course in Radiology for Radiologists will be given at the Center for Continuation

Study, University of Minnesota, Minneapolis, Minn., Nov. 6-10, 1961. The theme of the course will be Urologic Radiology.

FACULTY OF RADIOLOGY ROYAL COLLEGE OF SURGEONS IN IRELAND

The President, Vice-President, and Council of the Royal College of Surgeons in Ireland have inaugurated a Faculty of Radiology. It is proposed to hold examinations for the Fellowship of the Faculty, but in the first instance the Council will award a limited number of Fellowships to Radiologists (diagnostic and therapy) of Consultant Status who have been practicing Radiology for not less than ten years.

Persons who wish their claims to be considered should send full particulars to the Registrar, Royal College of Surgeons in Ireland, St. Stephen's Green, Dublin, before Jan. 1, 1962.

WORLD ASSOCIATION OF UNIVERSITY PROFESSORS OF MEDICAL RADIOLOGY

The World Association of University Professors of Medical Radiology (Director, Professor H. R. Schinz) will hold its next meeting in Zurich in October 1961.

Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

VERTEBRAL AND CAROTID ANGIOGRAMS IN TENTORIAL HERNIATIONS INCLUDING ROENTGEN ANATOMY OF THE TENTORIAL INCISURE. By HANS F. PLAUT, M.D., Chief, Radiology Service, Veterans Administration Center, Dayton, Ohio; Clinical Assistant Professor of Radiology, Ohio State University, College of Medicine, Columbus, Ohio; Formerly, Instructor in Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio. With a Foreword by Juan M. Taveras, M.D., Professor of Radiology, Columbia University, College of Physicians and Surgeons; Radiologist, Neurological Institute, Columbia Presbyterian Medical Center, New York. A volume of 156 pages, with 32 figures. Published by Charles C. Thomas, Springfield, Ill., 1961. Price \$10.50.

NEURORADIOLOGY WORKSHOP. VOLUME I: SCALP, SKULL AND MENINGES. By LEO M. DAVIDOFF, M.D., Active Consultant Neurosurgeon, Montefiore Hospital, and Professor and Chairman, Department of Neurosurgery, Albert Einstein

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College of Medicine, Yeshiva University, New York, HAROLD G. JACOBSON, M.D., Chief, Division of Diagnostic Radiology, Montefiore Hospital; Professor of Clinical Radiology, New York University School of Medicine, New York, and HARRY M. ZIMMERMAN, M.D., Chief, Division of Laboratories, Montefiore Hospital, and Professor of Pathology, College of Physicians and Surgeons, Columbia University, New York. A volume of 256 pages, with 89 figures. Published by Grune & Stratton, New York 16, N. Y., 1961. Price \$16.50.

PROTECTION AGAINST RADIATION: A PRACTICAL HANDBOOK. By JOHN D. ABBATT, M.B., Ch.B., D.M.R.; J. R. A. LAKEY, Ph.D., B.Sc., A.Inst.P., and D. J. MATHIAS. Foreword by J. S. Mitchell, C.B.E., M.A., M.D., F.R.C.P., F.F.R., D.M.R., F.R.S. A volume of 236 pages, with 48 figures. Published by Charles C Thomas, Springfield, Ill., 1961. Price \$6.50.

A MANUAL FOR NUCLEAR MEDICINE. By E. R. KING, Captain, MC, U. S. Navy, and T. G. MITCHELL, Lieutenant, MSC, U. S. Navy. With a Foreword by B. W. Hogan, Rear Admiral, MC, U. S. Navy, Surgeon General of the Navy. A volume of 406 pages, with 80 figures. Published by Charles C Thomas, Springfield, Ill., 1961. Price \$13.50.

PHLEBOGRAPHY AND VENOUS PRESSURE DETERMINATION: A STUDY INTO THE CORRELATION OF THE DATA GAINED FROM THESE METHODS. By M. N. VAN DER HEYDE, M.D. A volume of 96 pages, with 23 plates. Published by Charles C Thomas, Springfield, Ill., 1961. Price \$5.00.

CANCER OF THE NASOPHARYNX: ITS NATURAL HISTORY AND TREATMENT. By M. LEDERMAN, M.B., D.M.R., F.F.R., Deputy Director, Radiotherapy Department, Royal Marsden Hospital; Consulting Radiotherapist, The Royal National Throat, Nose and Ear Hospital, The Metropolitan Ear, Nose and Throat Hospital, Moorfields Eye Hospital, The Royal Eye Hospital, The Chelsea Hospital for Women, London, England. Publication No. 432, American Lecture Series. A monograph of 118 pages, with 53 figures. Published by Charles C Thomas, Springfield, Ill., 1961. Price \$6.75.

THE SPINAL CORD: BASIC ASPECTS AND SURGICAL CONSIDERATIONS. By GEORGE AUSTIN, Professor and Head, Division of Neurosurgery, University of Oregon Medical School; Chief Consultant in Neurosurgery, Veterans Administration Hospital, Portland, Oregon; Formerly, Assistant Professor of Neurosurgery, University of Pennsylvania, Philadelphia, Penna. A volume of

532 pages, with 362 figures. Published by Charles C Thomas, Springfield, Ill., 1961. Price \$26.50.

PROBLEMS OF INFECTION, IMMUNITY AND ALLERGY IN ACUTE RADIATION DISEASES. By N. N. KLEMPARSKAYA, O. G. ALEKSEYEVA, R. V. PETROV, and V. F. SOSOVA. Translated from the Russian into English by Lydia Venters, Argonne National Laboratory, Lemont, Ill. Translation editor: R. Clarke, B.Sc. A monograph of 166 pages, with 34 figures and 29 tables. Published with the assistance of the National Institutes of Health, Public Health Service, U. S. Department of Health, Education and Welfare by Pergamon Press, Inc., 122 East 55th St., New York 22, N. Y., 1961. Price \$7.50.

MAMMARY CARCINOMA: THE BIOLOGIC CHARACTER OF MAMMARY CARCINOMA STUDIED IN 517 CASES BY A NEW FORM OF MALIGNANCY GRADING. By K. A. HULTBORN and Bo TÖRNBERG. From the Institute of Radiopathology (Director: Prof. Lars Santesson), and Radiumhemmet (Director: Sven Hultberg), Karolinska Sjukhuset, Stockholm, Sweden. Acta radiol. Suppl. 196. A monograph of 144 pages, with 74 figures and 140 tables. Published by Acta radiol., Stockholm 2, Sweden, 1960. Price Sw. Kr. 55:—

THE MITOTIC AND RADIOPROTECTIVE EFFECT OF CYSTEINE AND LYSINE IN RAT. By LARS R. HOLSTI. From the Department of Pathology, Section II (Director: Prof. Harald Teir), University of Helsinki, Finland. Acta radiol. Suppl. 197. A monograph of 100 pages, with 17 figures and 18 tables. Published by Acta radiol., Stockholm 2, Sweden, 1960. Price Sw. Kr. 30:—

THE ISOMETRIC RELAXATION PHASE OF THE LEFT VENTRICLE: AN ELECTROKYMOGRAPHIC STUDY. By OSBORNE BARTLEY. From the Roentgen Diagnostic Department I (Head: Prof. Sven Roland Kjellberg, M.D.), and the Roentgen Diagnostic Department II (Head: Docent Ingmar Wickbom, M.D.), Sahlgrenska Sjukhuset, Göteborg, Sweden. Acta radiol. Suppl. 198. A monograph of 116 pages, with 49 figures and 14 tables. Published by Acta radiol., Stockholm 2, Sweden, 1960. Price Sw. Kr. 35:—

CONTRAST EXAMINATION OF THE CARDIOVASCULAR SYSTEM DURING INCREASED INTRABRONCHIAL PRESSURE. By BJÖRN NORDENSTRÖM. From the Department of Radiology (Director: F. J. Hodges), University Hospital, Ann Arbor, Mich., U. S. A., and from the Department of Experimental Surgery (Director: Å. Senning), and the Department of Roentgenology (Director: B. Nordenström), Thoraxkliniken, Karolinska Sjukhuset, Stockholm, Sweden. Acta radiol. Suppl.

200. A monograph of 110 pages, with 51 figures and 1 table. Published by Acta radiol., Stockholm, 2, Sweden, 1960. Price Sw. Kr. 30:—

RISA ENCEPHALOGRAPHY AND CONVENTIONAL NEURORADIOLOGIC METHODS: A COMPARATIVE STUDY. By GIOVANNI DI CHIRO. From the Neuroradiological Section (Director: Giovanni Di Chiro) of the National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Maryland, U. S. A. Acta radiol. Suppl. 201. A monograph of 102 pages, with 101 figures. Published by Acta radiol., Stockholm 2, Sweden, 1961. Price Sw. Kr. 35:—

LA GROSSE TUBÉROSITÉ DE L'ESTOMAC NORMALE ET PATHOLOGIQUE: ÉTUDE CLINIQUE ET RADIOLOGIQUE. By T. SCHOPS. Preface by Dr. René A. Gutmann. A volume of 574 pages, with 910 illustrations on 475 figures. Published by G. Doin & Cie, 8, place de l'Odéon, Paris VI^e, France, 1961. Price 125 NF.

LE NEOPLASIE MALIGNA DELLA TIROIDE: DIAGNOSI E TERAPIA. By FRANCO CHIARIOTTI, Ospedale di Circolo di Busto Arsizio. Sezione di radiologia (Primario: Prof. C. Picchio). Sezione di isotopi (Primario: Prof. U. Marinoni). A monograph of 188 pages, with 45 figures. Published by Minerva med., Turin, Italy, 1960. Price L. 3000.

Book Reviews

PEDIATRIC X-RAY DIAGNOSIS: A TEXTBOOK FOR STUDENTS AND PRACTITIONERS OF PEDIATRICS, SURGERY & RADIOLOGY. By JOHN CAFFEY, A.B., M.D., Director of Medical Education, Children's Hospital of Denver; Consultant Pediatrician, National Jewish Hospital at Denver, Colo.; Professor Emeritus of Radiology, College of Physicians and Surgeons, Columbia University; Consultant Radiologist, Columbia-Presbyterian Medical Center, New York, N. Y. A volume of 1,236 pages with 2,908 illustrations on 1,536 figures. Published by Year Book Publishers, Inc., Chicago 11, Ill., 4th ed., 1961. Price \$32.00.

The original edition of Caffey's Pediatric X-Ray Diagnosis appeared in 1945, the first textbook on the subject to be published in thirty-five years. Now, in a fourth edition, the author has brought this excellent text up to date, emphasizing the rapid development of this field in recent years. About 200 pages of text have been added to the original work. To quote directly from the author:

"The reader will find 127 new and important items which are depicted in 269 new figures which contain 644 prints. Some of the more important include 11 new variants in the skull, cranial changes in iron deficiency anemia and in cyanotic heart disease, dermoid of the nose, schematic drawings of the

maturation of the normal cervical spine, kyphosis and accelerated maturation of the sternum associated with congenital heart disease, eventration of the diaphragm in infantile cortical hyperostosis, tracheal bronchus, congenital adenomatoid malformation of the lung, pneumocystis carinii, proteinosis of the lungs, familial fibrocystic pulmonary dysplasia, steroid-induced atrophy and regrowth of the thymus, ectopic (right-sided) left pulmonary artery, corrected transposition of great arteries, Ebstein's malformation of the tricuspid valve, schematic drawings of the normal biliary and pancreatic ducts, intussusception of the esophagus into hiatal gastric hernia, dorsal enteric cysts and fistulas, progressive stages in reduction of ileocecal intussusception, obstructing meconium plugs, the pelvis in mongolism and achondroplasia, natural course of benign cortical defects, congenital constrictions and angulations in the extremities, dysplasia epiphysealis hemimelica, recurrent Perthes' disease, coxa plana due to staphylococcal osteitis, deep cupping of the distal femoral metaphyses after acute metaphysitis, chronic idiopathic hyperphosphatasia, multiple sclerotic osteogenic sarcomas, aneurysmal bone cysts, metastatic embryonal rhabdomyosarcoma, idiopathic chronic hypercalcemia, pulmonary osteoarthropathy in cystic fibrosis of the pancreas, a new section on rheumatoid arthritis."

The book remains invaluable as a reference source to the practicing radiologist. The resident in radiology will find it an informing and readable text.

CONGENITAL MALFORMATIONS OF THE HEART. VOLUME I: GENERAL CONSIDERATIONS. VOLUME II: SPECIFIC MALFORMATIONS. By HELEN B. TAUSSIG, M.D., Professor of Pediatrics, Johns Hopkins University School of Medicine; Physician-in-Charge, Cardiac Clinic, Harriet Lane Home, Johns Hopkins Hospital, Baltimore, Md. Vol. I: 204 pages; Vol. II: 1,050 pages, both with numerous figures. Published for the Commonwealth Fund by Harvard University Press, Cambridge, Mass., 1960, 2d ed. Price \$4.75 (Vol. I); \$17.50 (Vol. II).

Since the publication in 1947 of the first edition of Dr. Taussig's well known book (reviewed in Radiology 50:695, May 1948), the diagnosis and treatment of congenital heart disease has come of age. Angiography, which at that time was in its infancy, has established itself as an important adjunct in the determination of anatomical relationships. The refinements in electrocardiographic interpretation have become equally sophisticated. To embrace the new developments Dr. Taussig has expanded her book to two volumes. The work is an excellent survey of the subject of congenital heart disease based upon the author's extensive experience. The discussion of the clinical aspects and suggested approach to correction of defects are particularly worthwhile.

The embryology, physiology, and methods of investigation are summarized in Volume I. The specific anatomic malformations, including the variations in the major congenital lesions, are presented in detail in Volume II. There is a generous use of schematic drawings, amplifying the explanation of the altered anatomic and physiologic findings in the various defects. The radiographic and angiographic illustrations, however, are somewhat limited in scope.

This text will be of interest to the student who wishes a general review of the clinical and radiographic aspects of congenital heart malformations. It suffers somewhat in comparison with some of the more specialized radiologic texts on this subject.

THE PHYSICS OF RADIOLOGY. By HAROLD ELFORD JOHNS, M.A., Ph.D., F.R.S.C., LL.D., Professor of Physics and Professor of Medical Biophysics, University of Toronto; Head, Physics Division, Ontario Cancer Institute, Toronto, Canada. Publication No. 419, American Lecture Series. A volume of 768 pages, with numerous figures and tables. Published by Charles C Thomas, Springfield, Ill., 2d ed., 1961. Price \$23.00.

The Physics of Radiation Therapy, published in 1953, has been revised and enlarged to more than twice its size to become *The Physics of Radiology*. Additional subjects covered in the later text include diagnostic radiology, isotopes, protection, radiobiology, and rotation therapy. To each of these a single chapter of less than 50 pages is devoted, so that the discussions are necessarily brief. The field of radiation physics has become so broad that it is almost impossible to include all its branches in a single book without important omissions. Such an omission from the present text is the Quimby system of radium dosage, based on uniform placement of sources, although it is often used clinically.

One of the revisions consists in the conversion of all doses from roentgens to rads. In view of this, it is surprising to find conventional direction of current flow used throughout.

In spite of these minor criticisms, the book is a valuable addition to the radiological physics literature. The new material has added much to its value, but its greatest contribution is still the discussion of basic radiation physics. The lucid style of the first edition is again evident. The extensive bibliographies are a guide to further reading, the problems enable the reader to test his understanding of the preceding material, and the tables at the end of the book will be useful.

No radiology resident, practicing radiologist, or radiological physicist should be without a copy of this book at hand. It is one of the best texts on the subject available.

THE BASIC PHYSICS OF RADIATION THERAPY. By JOSEPH SELMAN, M.D., Clinical Assistant

Professor of Radiology, The Southwestern Medical School, University of Texas; Director, School for X-ray Technicians, Tyler Junior College; Chief of Radiology Service, Medical Center Hospital; Attending Radiologist, Mother Frances Hospital; Consultant in Radiology, East Texas Tuberculosis Hospital, Tyler, Texas. A volume of 672 pages, with figures and tables. Published by Charles C Thomas, Springfield, Ill., 1960. Price \$14.50.

The author has written a companion book to his *Fundamentals of X-ray and Radium Physics*. Again, he begins with simple mathematics and atomic theory, followed by chapters on the nature of radiation and the production of x-rays. Where the earlier book was directed to the student technician, with emphasis on diagnosis, the present volume is meant for the advanced technician, the radiology resident, and the practicing radiologist who wants a refresher course. The emphasis is on therapy, covering equipment, treatment planning, protection, and radiobiology.

It is a difficult thing to write a book that would be appropriate for so diverse a group as has been mentioned, and almost inevitably each member will be dissatisfied with the result. The over-simplification will be annoying to the reader seeking a refresher course, while the complexity of the concepts of radiation physics will discourage all but the exceptional technician. For the resident, too, there are other more appropriate texts.

RADIOISOTOPE TECHNIQUES IN CLINICAL RESEARCH AND DIAGNOSIS. By N. VEALL, B.Sc., F.Inst.P., Guy's Hospital Research Fellow; Honorary Research Physicist, Institute of Obstetrics and Gynaecology, University of London, London, England; Consultant Physicist, Plastic Surgery Centre, Salisbury, and H. VETTER, M.D., Head, Radioisotopes Laboratory, 2nd Medical University Clinic, Allgemeines Krankenhaus, Vienna, Austria. A volume of 418 pages, with 74 figures. Published by Butterworth, London, England, and Washington 14, D. C., 1958. Price \$10.00.

This volume on *Radioisotope Techniques* is an example of a happy collaboration between physicist and clinician in the discussion of the application of radioisotopes to medical problems. In general, the first part of the book presents the physics and the last part the clinical aspects of isotope techniques, but there is no sharp division between the two points of view. Basic physics has been kept to a minimum and the emphasis in the discussion of equipment is on its practical use to best advantage. The mechanics of single and multiple compartment systems are explained to illustrate the fundamental concepts and mathematical methods which are employed in tracer experiments. Established clinical examinations are described briefly but clearly, including interpretation of results. A good example of the

practical and simple approach is the section on assessment of radiation dosage and consequent risk to the patient.

A surprising amount of practical information is contained in this book. It should help the physicist to grasp the clinical problem better and the clinician to understand the physics involved. The word "practical" has been used repeatedly throughout this review because it is an outstanding characteristic of the book. It is this which makes the book still valuable some years after its first publication.

ANNUAL REVIEW OF NUCLEAR SCIENCE. VOLUME 10. Editor: EMILIO SEGRÈ, University of California. Associate Editors: GERHART FRIEDLANDER, Brookhaven National Laboratory, and WALTER E. MEYERHOF, Stanford University. A volume of 618 pages, with figures and tables. Published by Annual Reviews, Inc., Palo Alto, Calif., 1960. Price \$7.00 (U. S. A.); \$7.50 elsewhere.

As has been true of most of its predecessors, this tenth *Annual Review of Nuclear Science* deals with fields in pure science, of little interest to radiologists. The exceptions this time are the last three chapters, which cover cellular and vertebrate radiobiology. Data shedding light on mechanisms of various radiation effects on the cell are given in the first of these, and will be of interest to clinical radiologists and researchers in this field. The metabolism of internal emitters, taken up in the next chapter, is basic to recommendations for radiation protection in work with radioisotopes. Late effects, described in the final chapter, include life shortening, carcinogenesis, and genetics.

Letter to the Editor

THE RADIOACTIVE DISINTEGRATION CONSTANT, LAMBDA

To Dr. Howard P. Doub
Editor of Radiology

DEAR DR. DOUB

There is a misconception regarding the disintegration constant, lambda (λ) which seems widespread among radiologists, radiological residents, and not a few radiation physicists. In most texts the disintegration constant is defined as "the fractional change in number of atoms which occurs in unit time." This definition is correct only in the limiting case where the unit time interval is infinitely short. In all other cases, lambda may be a fraction or it may be a number greater than one; it is *never* the fractional change in number of atoms as given in the above definition.

Consider radon, whose half-life is 3.825 days. Its disintegration constant is $0.693/3.825 = 0.18$ per

day. In this case lambda is a fraction. However, it is equally justifiable to consider the disintegration constant per month. In this case the half-life of radon is 0.1275 months, and the disintegration constant is $0.693/0.1275 = 5.43$ per month, a number which is certainly not a fraction. Lambda will thus be either a fraction or a whole number depending on the half-life and the units in which it is expressed.

I have asked many radiologists, and a few radiation physicists, this question: "The decay constant of radon is 0.18 day^{-1} . What per cent of the atoms disintegrate per day?" The answer is invariably "18 per cent." This is not correct. The per cent of radon atoms disintegrating per day must be obtained from the equation $N = N_0 e^{-\lambda t}$. If N_0 is taken as 100, lambda as 0.18 day^{-1} , T as 1 day, then N equals 84, and 16 atoms out of 100 have decayed per day, or 16 per cent per day, *not* 18 per cent, as would be concluded from the common definition of the constant.

It is possible that this misconception has gone along so many years because in the above classical example, using radon, the correct and incorrect answers are so nearly alike that most persons have assumed a small arithmetic error somewhere along the line. It is not an arithmetic error at all; it is a philosophical error.

When the disintegration constant of radon is taken per day, the per cent disintegrating per day is about 11 per cent less than the constant. As the unit of time decreases, so does the error. The per cent of atoms decaying per hour is only about 0.5 per cent less than the constant. However, it must be realized that there will always be a difference until the unit of time becomes zero.

This misconception, which occurs even in the early radium literature, probably stems from a misuse of the basic differential equation $dN/N = -\lambda dt$. The left-hand term of this equation cannot be treated as an ordinary arithmetic fraction, which is done when lambda is defined as the fractional change per unit time.

Lambda may be thought of as a number, either a fraction or a whole number which is related to the rate of disintegration, but is the fractional change only in the limiting case where the time is zero. For all positive times, however short, lambda is defined properly by the equation:

$$\lambda = \frac{\log N_0 - \log N}{T \log e}$$

where N_0 is the number of atoms at time zero; N is number remaining after time T ; and $\log e$ equals 0.4343. Lambda and T must be in the same units.

Sincerely yours,
Robert S. Landauer, Ph.D.
Cook County Hospital, Chicago

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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

Glioblastoma Multiforme: A Clinical Survey. John G. Roth and Arthur R. Elvidge. *J. Neurosurg.* 17: 736-750, July 1960. (A.R.E., Montreal Neurological Institute, Montreal, Quebec, Canada)

During the period 1928-1953, 2,295 neoplasms of the central nervous system were examined in the Department of Neuropathology of the Montreal Neurological Institute. Of these, 1,289 were classified as gliomas and 506 as glioblastoma multiforme. The authors present an analysis of the clinical aspects of 495 cases of glioblastoma multiforme in which an adequate follow-up was obtained.

Four hundred and eighty-nine of the 495 patients had intracranial tumors, and reports of roentgenograms of the skull were available in 406 of these. The pineal gland was calcified in 43 per cent. It had shifted 3 mm. or more from the midline away from the site of the tumor in 90 per cent. Calcification of the choroid plexus was visible in 8 per cent of the cases; in 21 per cent there was erosion of the sella turcica and/or clinoid processes. Intracranial calcification, within the tumor, was present in 9 cases. Separation of the sutures was observed in 5 patients, 2 of whom were over thirty-two years of age.

Pneumography was used almost exclusively for localization of the tumors. Of 80 pneumoencephalograms, 2 were reported as normal. Of 316 ventriculograms, 2 were negative. This does not include air studies with insufficient filling. Some patients underwent surgery without ventriculography and in others both pneumoencephalography and ventriculography were performed. The third ventricle was visualized (by pneumography) in 105 patients with lesions of the temporal lobe. It was curved away from the site of the lesion in 54 per cent. By comparison, the third ventricle was visualized in 153 cases with the lesion situated in other than the temporal lobe. It was curved in only 11.7 per cent. A tumorous cyst was filled with gas during pneumography or ventriculography in 50 patients. Angiography was done in only 8 cases.

Surgical removal of the tumor was attempted in 399 patients. A relatively complete (gross) removal was reported in 59 per cent of the cases. The overall postoperative survival for the group operated upon averaged 10.3 months, with survival times ranging from zero to fifteen years.

In an attempt to determine the usefulness of roentgen therapy, the average postoperative survival and the percentage of patients surviving certain periods were computed for different groups. Some patients did not live long enough to receive roentgen therapy, while others were not considered "good candidates" for it. Therefore, the use of roentgen therapy implies selection and makes it difficult, if not impossible, to obtain comparable groups for evaluation. One hundred and sixty patients who did not receive roentgen therapy survived operation for an average of 9.8 months, while 144 who received roentgen therapy survived operation 17.4 months. A comparison of the percentages of patients surviving certain periods showed a rather large and consistent difference for all periods up to and including five years. The average postoperative survival for 67 patients whose tumors were incompletely removed and who received no roentgen therapy was 8.2 months. In

48 patients whose tumors were incompletely removed but who received roentgen therapy, the survival averaged 17.3 months. In 93 patients with apparently complete removal of the tumor and no roentgen therapy, the average postoperative survival was 10.9 months, while in 96 patients with apparently complete removal of the tumor and roentgen therapy, the average was 17.4 months. The percentages of survival with both complete and incomplete removal of the tumor showed a definite difference in favor of roentgen therapy at every postoperative period.

The prognosis appeared to be more favorable for patients under thirty-five and for females. It was considerably better for patients operated upon than for those who had biopsy or no operation. Patients with apparently complete removal of the tumor showed a longer average postoperative survival than those with a known incomplete removal. This, however, did not appear nearly so significant as the consistently better average survival associated with roentgen therapy.

Eleven tables.

Roentgenologic Study of Choroid Plexus Papillomas in Childhood. Francis D. L. Crofton and Donald D. Matson. *Am. J. Roentgenol.* 84: 479-487, September 1960. (D. D. M., 300 Longwood Ave., Boston, Mass.)

Papillomas of the choroid plexus constitute 3.9 per cent of the intracranial tumors of childhood seen at The Childrens Medical Center, Boston. The authors present the roentgenologic features of 16 cases observed between 1941 and 1958. A more complete analysis of this group of cases, together with a review of 67 cases in children recorded in the literature, appears elsewhere (*J. Neurosurg.* 17: 1002, 1960).

The average age in the present series was sixteen months. Only 1 child was over three. Fourteen papillomas were located in the atrial region of a lateral ventricle, 1 in the anterior portion of a lateral ventricle, and 1 in the fourth ventricle.

The clinical findings were meager and nonspecific, but the roentgenologic findings were usually diagnostic. Plain roentgenograms of the skull were invariably abnormal and in all but a single instance showed unequivocal evidence of increased intracranial pressure. Intracranial calcification in the tumor or elsewhere was not demonstrated roentgenologically in any case.

Ventriculographic findings were abnormal in all 16 patients and in most cases proved unequivocally diagnostic. An outstanding feature was the demonstration of hydrocephalus in every case except 1 of the series. In 9 patients the hydrocephalus was of the communicating type. In 6, there was actual obstruction of a portion of the ventricular lumen by the tumor itself. Usually, the lateral ventricle containing the tumor was slightly larger than the opposite one. In 11 cases there was a slight but definite shift of the ventricular system away from the side of the tumor. In 1 patient the tumor was located in the caudal part of the fourth ventricle, with marked symmetric enlargement of the lateral and third ventricles and enlargement of the fourth ventricle out of proportion to the rest of the ventricular system. In 12 patients the tumor itself was outlined on the ventriculogram as a rather irregular, homogeneous, polypoid soft-tissue density lying entirely within the ventricular lumen or completely filling a portion of it. The combination of an intraventricular

mass in the presence of communicating hydrocephalus is pathognomonic of papilloma of the choroid plexus, particularly if the ventricular fluid is xanthochromic or contains markedly elevated total protein. Three patients showed a porencephalic-like cyst on ventriculography, probably representing dilated, obstructed portions of the ventricle adjacent to the tumor site.

One patient was essentially moribund on admission and died before surgery could be carried out. The remaining 15 patients were operated upon. Three of these died subsequently from inoperable invasive tumors and 1 from gastric hemorrhage. Of the 11 surviving patients, 4 are retarded and 7 are developing well.

The prompt and permanent relief of increased intracranial pressure in all patients from whom a papilloma of the choroid plexus was successfully removed would seem to be evidence that the hydrocephalus was due solely to overactivity of the tumor.

Twenty-one roentgenograms.

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Contribution to the Question of Cerebral Vasospasm. H. Krayenbühl. Schweiz. med. Wchnschr. 90: 961-965, Aug. 27, 1960. (In German) (Neurochirurgische Universitätsklinik Zürich, Switzerland)

The occurrence of transient or permanent brain damage due to vasospasm is generally considered unlikely, as localized areas of brain softening are usually not accompanied by vascular occlusion. Furthermore, arteriosclerotic changes of the carotid and cerebral arteries do not give rise to vasospasm. Clinical manifestations such as transient paresis and aphasia are due to a hypotensive condition with delay of collateral circulation.

Cerebral arteriography, however, has shown that the larger cerebral arteries can become spastic and may respond to vasodilators such as procaine and papaverine. The spasm is usually secondary to brain trauma from a ruptured aneurysm and perivascular hemorrhage. Vascular crises are rare unless caused by organic arterial changes. Nevertheless, suddenly appearing transient paresis and postoperative hemiplegia can be explained on the basis of vasospasm. To prove this contention the author reports 3 illustrative cases.

In 2 cases temporary hemiplegia occurred a few days after removal of a pituitary adenoma and acoustic neurinoma, respectively. Both patients responded well to intensive papaverine medication. Carotid arteriography disclosed temporary narrowing of the internal carotid in one and of the anterior cerebral artery in the other patient. In the third case a spontaneous hemiparesis and aphasia lasted only three hours. Carotid arteriography revealed localized spasm of a right anterior cerebral artery branch. Fifteen months later an endarteritis was found in the same area. In all 3 cases collateral circulation brought about complete recovery.

Six roentgenograms.

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Circulatory Disturbances During Cerebral Angiography. An Experimental Evaluation of Certain Contrast Media. Erik Kågström, Percy Lindgren, and Gunnar Törnell. Acta radiol. 54: 3-16, July 1960. (Karolinska Institutet, Stockholm, Sweden)

The authors attribute the discrepancy in reactions

(vasoconstriction or vasodilatation) to cerebral angiography and the side effects reported to the lack of a simple and general means of recording cerebral blood flow and to widely different experimental conditions. Margolis *et al.* (J. Neurosurg. 15: 30, 1958. Abst. in Radiology 72: 127, 1959) compared the effects of several contrast media used in cerebral angiography and concluded that sodium acetrizate was the most toxic agent and sodium diatrizate least toxic, with other agents being intermediate. In an investigation of the cerebral blood flow in cats during carotid angiography with sodium acetrizate and sodium diatrizate, reported in 1958 (Acta radiol. 50: 151, 1958. Abst. in Radiology 72: 773, 1959), the authors found a marked increase of venous flow after injection of sodium acetrizate but no change following sodium diatrizate.

The experiments described here were performed to ascertain whether acetrizate does in fact have a constant vasodilator action on the cerebral vessels. The blood flow in the internal carotid was measured in 7 dogs before and after injection of 4 different contrast media in varying amounts (injection volumes ranged from 0.05 to 0.2 ml.). A direct method of measurement was employed, using a drop chamber with a photoelectric recording unit placed between the divided ends of the common carotid artery; all branches distal to the internal carotid were ligated, but the axillary and external carotid were connected by plastic tubing in an effort to maintain physiologic conditions as far as possible in the intra- and extracerebral circulations. The authors believe that this procedure has fewer drawbacks than the one previously used, where measurements were made of the venous flow in the sagittal sinus which drains parts of both hemispheres.

After injection of the various contrast media, routine carotid angiography was done; the injected material filled chiefly the ipsilateral vessels, with no major communication with the extracerebral circulation, which means that the method actually does record the magnitude of cerebral blood flow.

Sodium acetrizate (Triurol) in doses of 0.1 to 0.2 ml. produced an increase in blood flow of 200 to 400 per cent, lasting approximately twelve minutes. Iodopyracet (Umbradil) in the same doses had a weaker effect with an increase in most cases of 100 to 250 per cent for about six minutes. Sodium diatrizate (Hypaque) usually had only a slight effect on the blood flow, the increase never exceeding 100 per cent and the duration about two minutes. Sodium diprotrizate (Mikonal) had essentially the same effect as sodium diatrizate. With the doses employed, the effects of carotid angiography on the systemic blood pressure were relatively slight; only sodium acetrizate caused a transient fall of 15 to 25 mm. Hg.

It is open to question whether the clinically demonstrable side-effects can be correlated with the vascular reactions. Nevertheless, it is interesting that Broadbridge (Brit. J. Radiol. 29: 577, 1956. Abst. in Radiology 69: 449, 1957) encountered far less discomfort in patients examined with sodium diatrizate than in those in whom sodium acetrizate or iodopyracet was employed. According to the authors' results, sodium diatrizate had the least vascular effect of the three.

Five figures, including 4 roentgenograms; 1 table.

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Angiography of the Superior Sagittal and Transverse Sinuses. Leon Morris. *Brit. J. Radiol.* **33**: 606-613, October 1960. (Brook Hospital, Shooters Hill Road, London, S.E. 18, England)

The author describes a method of superior sagittal and transverse sinography. The value of the procedure is assessed on the basis of sinograms obtained in 100 normal cases, 2 cases of meningioma, and 4 cases of suspected sinus thrombosis. All patients in the "normal series" had carotid arteriography for some condition in which the venous sinuses were not involved in any pathological process. A roentgenogram of the venous phase was secured only in those cases in which an oblique view of the arterial phase was necessary. In other words, no contrast medium was injected other than that required in the investigation taking place. All that was done was to add one exposure, and all sinograms secured in the venous phase were obtained at this first attempt. In the majority of cases the oblique half-axial view was used; the exposure was made four to six seconds after commencement of injection of the contrast medium. Internal carotid puncture produced far more satisfactory superior sagittal sinograms (78 per cent) than did common carotid injection (42.4 per cent).

For transverse sinus venography it is necessary to alter the technic slightly, the film being exposed six to eight seconds after the beginning of the injection. The transverse sinuses were well visualized in only 18 of the 100 cases, due mainly to the timing of the exposures. They filled equally well in 50 per cent of these cases; left-sided dominance was demonstrated in 22 per cent, and right sinus dominance in 28 per cent.

The superior sagittal sinus drains mainly to the right transverse sinus and the straight sinus mainly to the left. In 22 per cent of normal cases one or the other transverse sinus may not opacify.

The conditions in which sinography is most likely to be useful are extradural hematoma, meningioma, sinus thrombosis, and hydrocephalus in children due to superior sagittal sinus obstruction.

Six illustrative cases are reported. In 2 cases of meningioma with bony involvement, sinusography showed obstruction of the right transverse sinus in one and patency of the superior sagittal sinus in the other. In 4 cases of suspected sinus thrombosis, sinograms revealed sinus obstruction in 2 and patency in the remainder. The 2 patients with patent sinuses had sustained injuries, and post-traumatic sinus thrombosis could be excluded as a cause of persistent symptoms.

Seventeen roentgenograms; 3 tables.

SAMUEL B. HAVESON, M.D.
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A Stereotaxic Technique in Man Allowing Multiple Spatial and Temporal Approaches to Intracranial Targets. Bertram Feinstein, W. Watson Alberts, Elwood W. Wright, Jr., and Grant Levin. *J. Neurosurg.* **17**: 708-720, July 1960. (Mount Zion Hospital, San Francisco, Calif.)

The authors describe (1) a method for localization of intracranial targets by precise stereotaxic means, (2) techniques for returning to the same or different target at later stages, on the basis of a single radiographic localization, and (3) a method for producing thermal lesions. The stereotaxic instrument designed by Leksell (1955) was used. This instrument translates the rectangular co-ordinate system of the localization procedure to the

spherical co-ordinate system employed for directing an electrode to a predetermined target. An advantage of this system is that an electrode may be directed to the target from any part of the calvaria through an infinite number of paths. A path may thus be selected to include structures that one may desire to investigate and to avoid structures that should be left undisturbed.

The current surgical technic involves two or more stages. In the first, the stereotaxic instrument is attached to the patient's head; radiographic procedures are employed to demonstrate reference structures in the brain and the instrument co-ordinate system. The reference structures now used are the anterior and posterior commissures and the midsagittal plane. By relating the radiographs obtained to a reference brain, the target is located in terms of the instrument's co-ordinate system. In subsequent stages an electrode is directed to the target, and a thermal lesion is produced.

Ten illustrations, including 1 roentgenogram.

Clinical Evaluation of Procaine and Hypertonic Glucose as Possible Adjuncts to Carotid Arteriography. George T. Tindall and James R. Jackson. *J. Neurosurg.* **17**: 43-48, January 1960. (Duke Medical Center, Durham, N. C.)

Experimental studies have demonstrated a remarkable protective effect of glucose and procaine against injury to the central nervous system by contrast media (*J. Neurosurg.* **15**: 92, 1958. Abst. in *Radiology* **72**: 141, 1959). This protection was achieved by injection of the selected vascular bed with large doses of one or the other of these agents immediately prior to the administration of the contrast material. The first aim of the investigation described here was to determine the physiologic effects in man resulting from intracarotid administration of glucose and procaine. The second was to establish whether this procedure affected the degree of filling of the cerebral vessels with contrast medium. Forty-five patients with the presumptive clinical diagnosis of acute subarachnoid hemorrhage or brain tumor were studied, with particular attention to the electroencephalographic, electrocardiographic, blood pressure, and radiographic changes.

The intracarotid injection of glucose produced no overt toxic or significant electroencephalographic or electrocardiographic changes. In 2 of 12 patients, a significant rise in arterial pressure occurred during injection. Arteriograms made at brief intervals following the administration of glucose, however, consistently showed diminished contrast of the internal carotid system. Because of this effect upon the diagnostic quality of the arteriogram, glucose cannot be employed as an adjunct to carotid arteriography.

The intracarotid administration of 20 to 100 mg. procaine produced seizures in 3 of 8 patients, and the agent was considered to be too toxic for further studies.

Four roentgenograms.

Hemicranial Aplasia with Pulsating Exophthalmos. An Unusual Manifestation of von Recklinghausen's Disease. Richard L. Rovit and Merrill C. Sosman. *J. Neurosurg.* **17**: 104-121, January 1960. (Montreal Neurological Institute, Montreal, Quebec, Canada)

It is becoming increasingly apparent that von Recklinghausen's disease is a diffuse, probably genetically established disorder with effects often manifest in the skin, peripheral and central nervous systems, and in bone. A characteristic but relatively rare abnormality

of the cranial vault has been reported in less than 50 patients with neurofibromatosis. In these cases there has been a unilateral agenesis of the sphenoid bone and posterior orbital bone often associated with atrophy of the ethmoid sinuses and outward bulging of the temporal bone on the affected side. The resulting skeletal defect in the orbit permits a unilateral pulsating exophthalmos to develop as a consequence of direct transmission of intracranial pulsations to the globe of the eye. The authors present 4 cases of this syndrome in an effort to alert clinicians and radiologists to this unusual manifestation of neurofibromatosis.

The distinctive facial appearance and characteristic roentgen findings in patients with hemicranial agenesis and pulsating exophthalmos should leave little doubt as to the diagnosis. Failure to recognize the anomaly may lead to an unnecessary intracranial or intra-orbital operation. In 2 of the authors' cases the initial diagnosis was congenital glaucoma. The affected eye was removed and a prosthesis was inserted in each case. As might be expected, the defect in the posterior orbit continued to transmit intracranial pulsations and both patients exhibited pulsations of their prosthesis synchronous with the cardiac cycle. In addition to the usual roentgenograms of the skull, tomograms in anteroposterior and lateral projections were obtained in all 4 cases. Carotid arteriography and pneumoencephalography were performed in 2 cases.

Nine roentgenograms; 5 photographs.

Skull Changes in Eighteen Cases of Dystrophia Myotonica. Giovanni Di Chiro and John Egerton Caughey. *Acta radiol.* 54: 22-28, July 1960. (National Institutes of Health, Bethesda, Md.)

Dystrophia myotonica is a hereditary familial disorder. When the disease first appears in a family, it presents as a cataract. This may be the only detectable evidence of the disease in one or several generations. Usually, however, in the second generation, the cataract develops at an earlier age and other features of the fully developed disorder appear, such as myotonia, muscle wasting, gonadal atrophy, frontal baldness, and cardiac abnormalities of conduction and rhythm.

The authors have summarized the findings in 18 cases of dystrophia myotonica, 16 with changes in the cranial vault. These changes were of four types: (1) thickened calvaria throughout, 9 cases; (2) thickened calvaria in the frontal region, 2 cases; (3) hyperostosis frontalis interna, 3 cases; (4) thickened calvaria throughout and hyperostosis frontalis interna, 2 cases. These "hyperostotic" changes of the vault occurred with equal frequency in males and females; this is in striking contrast to the predominance of the usual hyperostosis cranii in women (99 per cent). The more severe changes occurred in women, and the longer the duration of the disease the more advanced were the changes. In 8 patients with evidence of gonadal failure, the degree of hyperostotic changes was most marked.

In 3 of the 18 cases the shape of the skull was acromegaloid. In 7 cases the frontal sinuses were large; in 2 a large sphenoidal sinus was present.

One of the authors, in a previous publication (J. E. C.: *J. Bone & Joint Surg.* 40-B: 701, 1958), suggested that hyperostosis cranii, excessive sinus formation, and prognathism are acromegaloid features brought about by unrestrained activity of growth hormone released as a result of hypogonadal function. The present series lends support to this contention. Another possibility

is that the skull changes may be on a genetic basis, as a pleiotropic manifestation of a single gene or an expression of involvement of different genes.

Five roentgenograms; 1 table.

LAURENCE B. LEINBACH, M.D.
Bowman Gray School of Medicine

Cineradiographic Studies of the Collar-Immobilized Cervical Spine. Malcolm D. Jones. *J. Neurosurg.* 17: 633-637, July 1960. (University of California School of Medicine, San Francisco 22, Calif.)

Cineradiography was employed to study the effect on the cervical area of devices for immobilizing the cervical spine. In this study, 11 patients wore cervical collars of plastic, leather, or felt-stockinet. Two additional patients wore chin-occiput braces: 1 of these had had fusion of the lower 3 cervical segments for anterior subluxation of the 7th cervical on the 1st thoracic vertebra. All patients, except the one with fusion, were examined with and without the collar by standard views of flexion and extension. One patient was studied both without the collar and with three different heights of the anterior portion of the collar.

Complete immobilization is obviously not obtained by the usual felt-stockinet collar. The plastic collar produces somewhat more stability because of the greater vertical dimension and stiffness. For absolute restriction of movement, the head also must be immobilized. With chin-occiput braces, complete immobilization was not possible, since the braces permitted forward motion of the head, producing flexion in the mid and lower cervical segments. To eliminate extension of the mid cervical segment, the patient must be prevented from retracting the chin. The height of the supporting device determined the fixation of the upper cervical spine through restriction of motion of the head. In some patients a tremor was observed when the collar was not in place; this may be related in a collar-dependent individual to an attempt to splint the cervical area against discomfort induced by motion.

Ten roentgenograms.

THE CHEST

Effects of Pulmonary Hypertension on the Tracheobronchial Tree. Jesse E. Edwards and Howard B. Burchell. *Dis. of Chest* 38: 272-284, September 1960. (The Mayo Clinic, Rochester, Minn.)

The changes which occur in the tracheobronchial tree as sequelae to intrinsic diseases of the heart associated with pulmonary hypertension are discussed. The types of hypertension which affect the tracheobronchial tree may be separated into two general categories, *i.e.*, *with-out* and *with* elevation of left atrial pressure.

Pulmonary Hypertension Without Elevation of Left Atrial Pressure: The aorta and the proximal part of the left pulmonary artery lie in a relatively fixed space between the left side of the trachea and the left upper lobe bronchus and its branches. When the pulmonary arterial system is tense and distended from severe pulmonary hypertension, the left pulmonary artery has a tendency to push the aortic arch upward and to the right. As a result, the aortic indentation on the left side of the trachea may become more pronounced than normal. Although this tracheal change is not responsible for symptoms, it should be recognized, when identified on the roentgenogram, as a reflection of increased pulmonary arterial pressure.

Pressure by the aortic arch against the trachea may cause impingement on the left laryngeal nerve and hoarseness. Enlarged tense pulmonary arteries exert an indirect compressive effect on the trachea by way of the aorta and also may compress elements of the bronchi directly. The left main bronchus may show distortion and to the right.

One site of predilection for involvement is the bifurcation of the right main bronchus, where the right lower pulmonary artery lies between the right upper lobe bronchus above, the intermediate bronchus below, and the distal end of the right main bronchus to the left. The tense, dilated right lower pulmonary artery may push the two bronchial branches away from each other and compress them as well.

Pulmonary Hypertension With Elevation of Left Atrial Pressure: When the left atrial pressure is elevated, pulmonary arterial hypertension coexists. In addition to the changes described in the previous section, there is displacement of the structures by the atriomegaly. It is worthy of note that the effects on the major airways by the enlarged left atrium may be at least as pronounced as those caused by the altered pulmonary arteries. The several anatomic relations of the left atrium and the tracheal bifurcation are reviewed in an attempt to explain the observed changes. In adults, compression of the left main bronchus ordinarily produces no symptoms. In infants and children, it may be responsible for obstructive emphysema or atelectasis and recurrent pulmonary infection.

Eleven roentgenograms; 15 photographs; 7 photomicrographs.

JOHN P. FOTOPOULOS, M.D.
Northwestern University Medical School

Unusual Clinical and Roentgenographic Features of Pulmonary Infarction. Vogesh C. Arora, Harold A. Lyons, and Philip A. Cantor. *Am. Rev. Resp. Dis.* 82: 232-239, August 1960. (State University of New York, Downstate Medical Center, Brooklyn, N. Y.)

The diagnosis of pulmonary embolism and infarction is often difficult, and when the roentgenographic and clinical findings are unusual, the difficulty is compounded. Six cases of pulmonary infarction with somewhat bizarre clinical and roentgen manifestations are reported.

The first patient gave a history of cough with low-grade fever for one month and the expectoration of a small amount of fresh blood on the day of admission to the hospital. A chest roentgenogram revealed an exudative parenchymal infiltration in the posterior segment of the right upper lobe. Although a diagnosis of pulmonary tuberculosis was not substantiated by laboratory tests, the patient was placed on antituberculosis drugs; later pneumoperitoneum was induced. Serial roentgenographic studies showed a continued increase in the size and extension of the area into the apical segment of the lower lobe; tomography indicated the presence of at least two cavities. It was thought that the patient had tuberculosis with a coexisting pulmonary neoplasm. A year following the first admission, the apical and posterior segments of the right upper lobe were resected. Pulmonary infarction was discovered, with no evidence of tuberculosis or neoplasm.

The second patient gave a two-day history of cough, chest and shoulder pain, chills, and fever. A chest roentgenogram showed consolidation of the posterior segment of the right upper lobe; tomography revealed a cavity containing a large, dense mass, suggestive of a

fungus ball. Exploration disclosed a pulmonary infarct with abscess formation, within which was a loose ball of necrotic lung tissue.

The third patient had had a temperature of 103° F. for three days and severe dyspnea for four weeks. No other symptoms were present. A chest roentgenogram was interpreted as showing a caseopneumonic infiltration of the left upper lobe with two cavities. A bronchogenic spread to both lower lobes was also noted. Antituberculosis therapy was instituted. The following day acute left ventricular failure developed and the patient died on the sixth day of hospitalization. Autopsy showed the lumen of the right pulmonary artery to be partially obstructed by a thrombus; another thrombus partially obstructed the left pulmonary artery. A thin-walled cavity in the left apex resulted from necrosis in the area of infarction.

Two patients gave a history of dyspnea of recent onset. The first had had pulmonary tuberculosis, and a chest roentgenogram taken on admission showed a well defined nodular density in the superior segment of the right lower lobe which had not been apparent on earlier examinations. This was thought to represent a bronchogenic carcinoma. The patient's condition rapidly worsened and he died within three weeks. Autopsy disclosed pulmonary tuberculosis with complete destruction of the left lung and an infarcted middle lobe. The other patient also had a cough in association with the dyspnea. A chest roentgenogram showed a small nodular density at the right base and extensive cavitory and necrotic disease of the left upper lobe. Postmortem examination revealed multiple pulmonary infarctions with necrotic abscesses.

The sixth patient was admitted with a temperature of 103° F. which was attributed to wound infection following a cholecystectomy. Roentgen examination revealed a moderately well circumscribed density in the anterior segment of the left upper lobe which was thought to represent segmental pneumonia or possibly bronchogenic carcinoma. A resection of the left upper lobe was performed and the pathologist found that the lung specimen contained a pulmonary infarction.

The classical symptoms of pulmonary infarction, *i.e.*, pleuritic pain, cough, and hemoptysis, and the typical electrocardiographic changes are more often absent than present. The history is not always characteristic and may actually suggest a chronic disease process. Since pulmonary infarctions are apparently becoming more frequent and are associated with such serious consequences and high mortality, it is important to bear in mind their unusual features.

Eleven roentgenograms. JOHN H. JUHL, M.D.
University of Wisconsin Medical School

Radiological Examination in Pulmonary Fibrotic Lesions. F. Fugazzola. *Minerva med.* 50: 1502-1517, May 16, 1959. English translation in *Panminerva med.* 2: 412-426, September 1960. (Istituto di radiologia dell'Università di Torino, Italy)

The author reviews the subject of radiological examination in pulmonary fibrotic lesions. These are seldom exclusively fibrotic, but are generally side phenomena of parenchymal alterations, often inflammatory in one stage of evolution.

In the solution of the clinical problems of fibrosis, all the means at the disposal of the radiologist should be employed: bronchography, stratigraphy, stereoradiography, pneumoangiography, and roentgen kymog-

raphy. It is important that the normal picture of the lung be well known. The roentgen signs unfortunately are not specific for the various fibrotic forms but are common to all of them, although there are some nuances which cannot always be seen or assessed. Radiological investigation, therefore, while of primary importance in identifying the nature and extent of the process, even if the causes have not been ascertained, must be supplemented by other clinical procedures.

An opinion on the disease that causes the fibrotic appearance can be formed on the basis of the systematic study of the shadows, according to whether their tone and dimensions are uniform, whether they are different or associated with other pulmonary disease findings, and whether they are localized in particular regions of the lung: hills, bases, or apexes. These simple assessments may be of value also for a differential diagnosis.

The possibility of obtaining the clinical diagnosis more easily in the future probably rests with radiography.

Thirty-one roentgenograms.

Bullous Emphysema. A Long-Term Study of the Natural History and the Effects of Therapy. Daniel J. Stone, Arthur Schwartz, and James A. Feltman. *Am. Rev. Resp. Dis.* 82: 493-507, October 1960. (VA Hospital, Bronx, N. Y.)

A long-term study was carried out on 15 male patients with bullous emphysema. Initial selection was on the basis of abnormal chest roentgenograms, with one or more bullae occupying at least one-quarter of the volume of one lung. Analysis of the histories of the 15 patients revealed no consistent pattern in regard to race, occupation, childhood disease, or previous acute respiratory disease. The age range was from twenty-three to forty-five years. Twelve of the patients had smoked for at least ten years prior to this study, 9 of them a minimum of 30 cigarettes daily. Three patients smoked irregularly or not at all.

Ten of the patients were asymptomatic when the emphysema was first detected on a routine chest roentgenogram. In 7 of this group, physical signs of wheezing, rhonchi, and coarsening of breath sounds developed relatively early in the study; these were attributed to bronchitis. Four patients sought medical attention because of symptoms of bronchitis (cough, bronchorrhea, intermittent wheezing, and dyspnea), while in the remaining patient the diagnosis was made at the time of a spontaneous pneumothorax.

At the time of admission to the study, roentgen examination showed bullous disease occupying one-quarter of the roentgenographic volume of one lung to three-quarters of the total volume of both lungs. In all but 1 case, the bullae were located predominantly in the upper lung fields. Air trapping was noted during forced expiration, with a mediastinal shift demonstrated in 12 patients. Serial roentgenograms indicated progressive enlargement of the majority of the bullae. The initial chest films of 12 patients revealed very small apical bullae in 7; in 4 there was a gradual appearance of bullae; in 1 almost complete bullous involvement of the left side was present from the beginning but was not recognized at first because of the remarkably homogeneous loss of normal "markings" on the affected side.

The results of pulmonary function studies, which were performed on all patients, are given in two tables. No consistent relationship between gas exchange and

ventilatory abnormalities was noted. Differential bronchspirometry revealed a significant reduction in the oxygen consumption of the involved lung in patients with unilateral bullae. In all patients in whom both differential bronchspirometry and angiocardigraphy were done, there was excellent correlation between the lack of vascularization and the reduction in oxygen consumption on the side containing the major bullae.

Ten patients underwent one or more surgical procedures, with resection of single or multiple bullae in each instance. In all patients treated surgically, a fixed mediastinum developed. This was accompanied by fluoroscopic evidence of significant improvement in diaphragmatic motion and marked diminution of air-trapping. Significant enlargement of remaining bullae occurred postoperatively in only 2 patients.

The basic abnormality in bullous emphysema seems to be an imperfect bronchiolar communication which permits air-trapping and overdistention of isolated areas of pulmonary parenchyma. The most striking evidence for the existence of this communication is the demonstration histologically of bronchioles entering bullae in all resected specimens. All sections revealed infiltration of bronchiolar walls with chronic inflammatory cells.

It is obvious that multiple etiologic factors may play a role in either the development or function of the imperfect bronchial communication. In view of the high incidence of chronic bronchitis, the apparent infrequency of giant bullous emphysema is not satisfactorily explained. In the authors' opinion, the relationships between chronic bronchitis and generalized obstructive emphysema are more convincing. Chronic bronchitis alone is not believed to be the cause of the inflammatory process.

Serial observations in some patients in the present series suggest that medical therapy designed to control bronchial inflammation may be of definitive value in the management of the patient with bullous emphysema. It has also proved of adjunctive value in surgically treated patients.

Eight roentgenograms; 3 tables.

JOHN H. JUHL, M.D.
University of Wisconsin School of Medicine

Etiology of Chronic Bronchopathies. Statistical Study of 252 Cases. G. Decroix, R. Pieron, and L. Mandonnet. *J. franç. de méd. et chir. thorac.* 14: 397-408, 1960. (In French) (Hôpital Saint-Antoine, Paris, France)

In a study of 252 patients with chronic bronchopathies the most important though probably not the only etiologic factors appeared to be allergy, chronic irritation, and infection. In this paper the allergic factor is given special attention.

The patient's history may indicate some allergic factor in the background. Eosinophils in the peripheral blood or in a bronchial biopsy are suggestive of this origin. Evidence of bronchospasm may be noted during bronchoscopy or during pulmonary functional studies. Skin tests may reveal other allergic factors.

In 122 patients studied from this point of view, 88.5 per cent showed at least one criterion and 50 per cent several criteria indicative of allergy in the etiologic background.

Eight graphs.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Vol. 77

Hypertrophic Pulmonary Osteoarthropathy. G. Lion. *J. belge de radiol.* 43: 417-444, 1960. (In French) (Institut médico-chirurgical du cinquantenaire, Bruxelles, Belgium)

The author reports 2 personal observations of hypertrophic pulmonary osteoarthropathy and, after comparing his cases with others published in the literature, draws the following practical conclusions:

1. Carcinoma of the lung is probably the sole etiologic factor of hypertrophic pulmonary osteoarthropathy; tuberculosis and other forms of pulmonary infection are only added or predisposing factors.
2. These tumors are very radiosensitive.
3. Radiologically a picture of osteoporosis is always associated with the periosteal changes.
4. Clinically the symptoms seem to progress in a fairly chronological order: clubbing of the digits is first observed, followed by osteoarthropathy and afterward by pulmonary manifestations.

According to an hypothesis offered by the author, the syndrome might be caused by a neurosympathetic excitation at the thoracic level which brings about a hyperpituitary reaction in patients with acromegaly tendency; it is this hyperfunction of the anterior pituitary gland which would trigger the osteoperiosteal syndrome.

Twelve roentgenograms; 2 photographs.

RENÉ HOURI, M.D.
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Pulmonary Manifestations of Boeck's Sarcoid (Radiographic and Stratigraphic Observations). G. Porro and P. Pierotti. *Radiol. med. (Milan)* 46: 559-568, June 1960. (In Italian) (Istituto di Radiologia dell'Università di Genova, Italy)

Clinical signs of pulmonary localization of Boeck's sarcoid, including functional abnormalities, are rare in the initial nodular and reticular varieties, whereas signs of respiratory insufficiency (dyspnea, cough, cyanosis) are present with massive involvement and emphysema. Microscopically a reticular lymphangitis, which is probably the substrate of the reticular pattern noted radiologically, is almost constantly present.

A useful classification of pulmonary involvement recognizes three forms: (1) The *miliary* or *micronodular* form is rarely pure. Apices and bases are spared, and there is confluence in the hilar area, with or without adenopathy. (2) In the *macronodular* form the foci are well delineated, of unequal size, and do not have the regular distribution of a tuberculous process. (3) The *reticulonodular* form is the commonest and the most characteristic. This represents a combination of macro- and micronodularity with striatal opacities, forming a coarse network.

The chronology of these three varieties is not definite and, although the macronodular and reticular varieties can derive from the micronodular variety, all types may appear together as the first manifestation of pulmonary involvement. In some patients the changes may disappear completely, either spontaneously or following medical treatment. In others they may persist in spite of treatment. In a third group, they may evolve into massive infiltrates with irregular contours, the so-called mediastinal-pulmonary variety. It is therefore obvious that the evolution of pulmonary changes cannot be predicted, although the majority clear within a short time (months or a few years). More or less dense foci of fibrosis corresponding to the regressing or regressed

circumscribed granulomatous formations may often supervene in the course of the disease. This fibrosis is especially perivascular and interstitial. The interalveolar septa are thickened by hyalinized connective tissue poor in cells.

The authors present 4 cases with stratigraphic observations.

Ten illustrations. CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Initial Respiratory Manifestations of Systemic Lupus Erythematosus: 3 Cases. J. Vidal, J. Mirouze, J. Salager, and J.-J. Guin. *J. franç. de méd. et chir. thorac.* 14: 557-567, 1960. (In French) (Montpellier, France)

Changes in the kidneys represent the usual predominant visceral change in systemic lupus erythematosus. However, abnormal findings in the lungs and pleura occur rather commonly and in some patients may constitute the initial symptoms of the disease. Pericardial effusion and ascites may also be noted in systemic lupus, creating a polyserositis. The pulmonary changes may regress but often are accompanied by renal changes which indicate a more serious prognosis.

Three cases are reported.

Four roentgenograms; 2 photomicrographs.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Wegener's Syndrome. Case with Unusual Features. Elizabeth H. Reeves, Albert DeGroat, and Paul T. Chapman. *Am. Rev. Resp. Dis.* 82: 394-399, September 1960. (Herman Kiefer Hospital, Detroit, Mich.)

A case is reported which presented the essential features of Wegener's syndrome: an initial nasal infection followed by fever, leukocytosis, eosinophilia, anemia, cutaneous eruptions, arthropathy, and terminal nephritis. Destruction of the nasal cartilage resulted in a characteristic "saddle nose" deformity. A chest roentgenogram revealed a large rounded mass in the left upper lobe just below and lateral to the left hilus, which was thought to be either a lung abscess or, more likely, a bronchogenic carcinoma. For this reason a left upper lobectomy was performed. The patient died poorly postoperatively and died in uremia about two months later. It was only after the autopsy findings were correlated with the patient's history and the roentgen findings that the true nature of the condition became apparent, and a diagnosis of Wegener's syndrome was made. In this case the granulomatous lesions were dominant and the vascular lesions few and only demonstrable by a careful search.

One roentgenogram; 4 photomicrographs.

JOHN H. JUHL, M.D.
University of Wisconsin Medical School

Intrathoracic Hibernoma. Carl J. May, Nicholas D. D'Esopo, and Raymond Yesner. *Am. Rev. Resp. Dis.* 82: 555-560, October 1960. (VA Hospital, West Haven, Conn.)

The hibernoma is a rare type of lipoma in which the fat is brown rather than the usual yellow. Distribution of hibernomas is similar to that of fat in hibernating animals. The authors point out that the term hibernoma is a misnomer, since the brown fat does not control hibernation and it is not clear whether the brown fat found in man is the same as that in the glands of hibernating animals, despite microscopic similarity.

Roentgenographically the hibernoma is slightly more dense than the usual lipoma because of its vascularity and the high percentage of phospholipid and glycogen.

The authors report what is believed to be the thirty-ninth case of hibernoma to be recorded and the fifth to be found in the thorax; the 4 previous cases of thoracic hibernoma are reviewed briefly. In the authors' case, the presenting symptoms were due to an incidental upper respiratory infection. Roentgenograms of the chest revealed a smooth, well circumscribed shadow at the level of the left fourth rib posteriorly. Planigrams gave the impression that the lesion was attached to the chest wall and was not in the lung, and this impression was confirmed by diagnostic pneumothorax. The patient was followed for four years, during which time the tumor grew slowly. In 3 of the 4 cases in the literature followed by serial roentgenograms, a slow growth of the tumor was also demonstrated. The preoperative diagnoses in the authors' case were mesothelioma and neurofibroma. The tumor was excised and proved to be a hibernoma.

Eight illustrations, including 3 roentgenograms.

JOHN H. JUHL, M.D.
University of Wisconsin School of Medicine

The Estimation of Maximal Breathing Capacity by Means of Chest Fluoroscopy and Inspiratory Roentgenograms. A Study in Patients with Pulmonary Tuberculosis. Gordon L. Snider and Allan R. Shaw. *Am. Rev. Resp. Dis.* 82: 314-321, September 1960. (Michael Reese Hospital, Chicago, Ill.)

An analysis was carried out, with standardized procedures, of the accuracy of estimation of maximal breathing capacity from fluoroscopy of the chest and from the frontal chest roentgenogram in 200 patients with pulmonary tuberculosis. The patients comprised two groups of 100 each, separated by an interval of more than two years. In addition to fluoroscopy, all patients had inspiration and expiration chest roentgenograms and at least maximal breathing capacity and vital capacity determinations.

It was found that the mean error of roentgenographic estimate was significantly greater than that of the fluoroscopic estimate. The mean error of fluoroscopic estimation for all 200 patients was 11.5 per cent, as compared with a roentgenographic error of 17.1 per cent. There was a decided tendency to underestimate function from the roentgenogram. The skill of the fluoroscopist improved as evidenced by a mean error of fluoroscopic estimate of 9.6 per cent in the second 100 patients as compared with an error of 13.1 per cent for the first 100.

The authors conclude that fluoroscopy of the chest is a cheap, readily available, and highly useful method for screening ventilatory function. It is significantly more accurate than estimates made from frontal chest roentgenograms, but it does not have sufficient accuracy to replace ventilatory function tests when precise information is needed.

Three figures; 2 tables. JOHN H. JUHL, M.D.
University of Wisconsin Medical School

Aimed Bronchography. D. Kassay, M. Erdelyi, and R. Schuster. *Dis. of Chest* 38: 382-390, October 1960. (Lankenau Hospital, Philadelphia, Penna.)

The authors describe a method of selective bronchography which entails insertion of special tubes at or near the desired bronchial orifice, under bronchoscopic

and fluoroscopic guidance. This has proved more satisfactory than "blind" introduction of curved tubes. Tubes have been made for four different types of cases; some are quite rigid but pliable, while others are flexible but hard enough to permit insertion into the narrowed lumen through the bronchoscope.

Aimed bronchography is meant to supplement not supplant routine bronchography. It is indicated in every case in which the routine bronchogram shows poor filling or the "dead tree effect" involving a pulmonary unit (lobe or segment). It was employed in 41 cases in a two-year period, sometimes with surprising results. Five cases are reported.

In addition to its diagnostic value, aimed bronchography may occasionally prove to be a therapeutic procedure, as demonstrated by one of the authors' cases in which an aspirated foreign body was expectorated with the contrast material and resulted in cure of an abscess which had persisted for five years.

Twenty-six roentgenograms; 1 photograph.

MAJ. MARTIN A. THOMAS, M.C.
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THE HEART AND BLOOD VESSELS

Thoracic Aortography. A Symposium. Brit. J. Radiol. 33: 531-567, September 1960.

At the British Institute of Radiology on April 7, 1960, a symposium on thoracic aortography was held, comprising four papers. Abstracts of these contributions follow.

I. Thoracic Aortography in Adults—Technical Aspects. Duncan McC. Gregg. *Brit. J. Radiol.* 33: 531-545, September 1960. (Addenbrooke's Hospital, Cambridge, England)

The author discusses the technical aspects of thoracic aortography, mainly in adults.

Indirect aortic opacification may be carried out from the right by venous angiocardiology or by injection of the contrast medium through a catheter from the pulmonary artery. Or the aorta may be opacified from the left by left ventricular needle puncture or by trans-aortic left ventricular catheterization.

Direct aortic opacification by parasternal and sternal needle puncture and intra-aortic balloon catheterization is not very practical. Catheterization techniques are more important. These may be (1) nonselective, with opacification of the entire aorta; (2) segmentally selective, with localized contrast filling of a segment of aorta adjacent to the catheter tip; (3) selective, by selective catheterization arteriography of arterial trunks, patent ductus, and aneurysms. Insertion of catheters into the aorta from femoral, brachial, radial, or carotid arteries may be facilitated by use of arterial needles and guide wires. Cardiac catheters which are a little stiffer than the soft polythene catheters sometimes used may be more useful when manipulation is difficult; they may be introduced by the percutaneous method of Seldinger insertion. With an image intensifier a catheter can be rapidly manipulated to the correct intra-aortic or intra-arterial position, and roentgenograms made after injection of the contrast medium.

The author discusses in detail preparation of the patient for these examinations, techniques for selective and nonselective catheterization, choice of contrast medium, and the complications of arterial and aortic catheterization.

It is recommended that the procedures be performed only in properly equipped centers and by experienced operators. "The prudent radiologist practising any form of angiocardiology should be well versed in measures to be adopted in the case of cardiac arrest. . . and should be capable of performing a thoracotomy and initiating cardiac massage if the occasion arises."

Thirty-three roentgenograms; 3 diagrams; 1 photograph; 2 tables.
DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

II. Thoracic Aortography in Adults—Clinical Aspects.

David Sutton. *Brit. J. Radiol.* **33**: 545-558, September 1960. (St. Mary's Hospital, London, W. 2, England)

The author's experience with thoracic aortography has been limited to percutaneous techniques, and with few exceptions all examinations have been carried out under local anesthesia with basal narcosis.

In 84 examinations on 75 patients, 35 aneurysms were diagnosed, 20 congenital lesions, and, in a lesser number, thrombosis, tumors and cysts, angioma, arteriovenous fistula, aortic valve disease, and coronary disease. Seven dissecting aneurysms of the thoracic aorta were seen. Several pseudoaneurysms due to the kinked artery syndrome were encountered. One parathyroid tumor was localized by transfemoral catheterization of the subclavian artery. In 2 cases thrombosis of major vessels arising from the aortic arch (which is said to be rare) was demonstrated. Three cases of traumatic arteriovenous fistula involving vessels at the base of the neck were investigated. One case was encountered in which the diagnosis was possible only by aortography because the lesion, although intrapulmonary, was an angioma of the systemic circulation.

The roentgenograms accompanying this article are excellent, and 5 brief summaries of interesting representative cases are presented.

Forty-two roentgenograms.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

III. Thoracic Aortography in Infants and Young Children.

R. E. Steiner. *Brit. J. Radiol.* **33**: 559-567, September 1960. (Hammersmith Hospital, London, W. 12, England)

In infants and young children counter-current or retrograde aortography is regarded as the method of choice for opacification of the thoracic aorta.

In young infants given preliminary sedation the brachial artery in the antecubital fossa is exposed under local anesthesia. A short length of polyethylene tubing is threaded 3 to 4 cm. into the artery, and the injection of contrast medium is made by hand with a standard 5-cc. Luer-Lok syringe. In slightly older children the catheter is advanced by way of the brachial artery into the subclavian artery, where injection is made, or catheterization can be carried out from the femoral artery, with advancement into the thoracic aorta, which is a more satisfactory approach. The position of the catheter will need to be appropriately adjusted for investigating patent ductus arteriosus, coarctation, aortic valve incompetence, etc. A pneumatic injector is employed. The circulation is very fast in young children, and 6 radiographic exposures per second for three to four seconds are needed, the first being made just before the injection is begun.

Of the indications for thoracic aortography, patent ductus in very small infants is the most important; it may be demonstrated clearly, particularly in a lateral

view. Aortography is not often required for the diagnosis of coarctation, since surgical repair is rarely indicated in this age group.

Retrograde left ventricular angiography may be indicated in the investigation of mitral incompetence and septal lesions and may be of great help in assessing the patient for surgery. The approach to the left ventricle by catheter or polyethylene tube is through the thoracic aorta and the method of examination is similar to that for thoracic aortography.

The principal source of error in interpretation of the aortograms seems to be poor filling of the aorta with contrast medium.

Twenty-one roentgenograms; 1 table.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

IV. Thoracic Aortography and Cineradiography of the Aortic Valve.

K. E. Jefferson. *Brit. J. Radiol.* **33**: 567-576, September 1960. (St. George's Hospital, London, S.W. 1, England)

Fifteen patients with aortic valve disease were studied by thoracic aortography and cineradiography to assess the degree of aortic incompetence. The catheter tip was positioned under intensifier screen control 2 to 3 cm. above the aortic valve. Injection of the contrast medium was made with a pneumatic injector during diastole. (If aortic incompetence is present, the regurgitant jet into the ventricle consists of pure opaque medium. If injection into the aorta occurs in systole, the regurgitation into the next diastole consists of opaque medium diluted with ejected blood from the left ventricle.)

A number of cineradiograms are reproduced, showing the anatomy of the normal aortic valve and the appearance of the valve in slight, moderate, and severe incompetence.

While the main value of cine-aortography lies in grading the degree of aortic incompetence, it is helpful also in differentiating between congenital and acquired valvular stenosis, except when superimposed atherosclerotic changes have thickened and distorted a congenitally stenotic valve, making it indistinguishable from an acquired lesion. The procedure makes possible, also, the exclusion of aortic incompetence in patients with mitral stenosis with pulmonary hypertension; this is of considerable importance because of the therapeutic implications. A patient with mitral stenosis with high pulmonary pressure should benefit from mitral valvotomy. On the other hand, there is good evidence that an incompetence may increase after valvotomy, resulting ultimately in left ventricular failure.

Forty cineradiographs; 1 drawing.

DON E. MATTHIESEN, M.D.
Phoenix, Ariz.

A Critical Review of Our Experience with Translumbar Aortography.

Parke G. Smith. *West. J. Surg.* **68**: 309-311, September-October 1960. (Mercy Hospital, Miami, Fla.)

Despite its title, this paper is primarily an analysis of the complications encountered in translumbar aortography. It is based on McAfee's survey of more than 13,000 abdominal aortographic examinations (*Radiology* **68**: 825, 1957) and 1,500 examinations performed by the author. In McAfee's collected series the mortality rate was 0.28 per cent and the morbidity rate 0.74

per cent, for an overall complication rate of 1.02 per cent. No serious complications occurred in the author's own series. His suggestions for prevention of complications are in general similar to those offered by McAfee. The author has performed all of his examinations under local anesthesia, but he recommends that general anesthesia be employed. McAfee believes that local anesthesia is indicated in most patients to minimize the danger of neurologic damage.

Aortography has been found useful in the preoperative study of congenital anomalies of the upper urinary tract, in hydronephrosis, and in cases of hypertension of possible unilateral renal origin. The author concedes that the aortographic findings may be misleading in renal infarction. Although the typical tumor pattern is frequently obtained, it is often extremely difficult to differentiate a cyst from a parenchymal tumor on the translumbar aortogram. In patients with blockage of the distal aorta, aortography should be limited to special cases in which specific information is necessary in order to plan treatment. JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Percutaneous Retrograde Selective Aortography.

Faber F. McMullen, Jr., Henry Goodwin Glass, and Eugene Cornelius. Texas State J. Med. 56: 779-782, October 1960. (Hermann Hospital, Houston, Texas)

For percutaneous retrograde selective aortography the authors used Teflon electronic insulating tubing. This material is tough, malleable, smooth, and relatively heat-resistant. It can be sterilized in the autoclave and re-used; many of the authors' catheters had been used six times and remained intact after a total of one hour of autoclaving in eight-minute periods. Multiple holes can be made near the tip of the catheter to reduce injection time and to prevent displacement of the catheter tip by jet effect. Modifications can be made in the catheter shapes and placement, depending on the individual requirements.

Accurate placement of the contrast medium and the effectiveness of small volumes of less concentrated contrast material make the authors' method desirable and relatively safe. The technic can be used in the demonstration of diseases in the arterial structures, in the intra-abdominal viscera, and in structures in the retroperitoneal area, or of tumors of the gastrointestinal tract. It is believed that selective percutaneous arterial catheterization will have many uses, spanning the fields of angiography, selective tumor perfusion, hemodynamic studies, and other diagnostic and therapeutic measures.

Seven roentgenograms; 1 photograph; 2 diagrams.

Atrial Septal Defect. M. M. Zion, B. A. Bradlow, and J. L. Braudo. South African M. J. 34: 810-817, Sept. 17, 1960. (Johannesburg, Union of South Africa)

The clinical, electrocardiographic, phonocardiographic, radiologic, and hemodynamic features of 43 cases of atrial septal defect are described. Thirty-seven of the patients had an isolated atrial septal defect and 6 a persistent common atrioventricular canal. The diagnosis was supported by cardiac catheterization in 28 patients and in 7 additional cases it was confirmed at necropsy. For purposes of discussion, the authors classify the cases into only two groups: (1) *Septum secundum defects* in which the atrial defect is in the general position of the foramen ovale, with intact ven-

tricular septum and normal atrioventricular valves; (2) *Septum primum defects*, which are always low and are frequently associated with congenital anomalies of the valves.

Atrial septal defect is a serious congenital anomaly with a high mortality in early infancy and early middle age. Such septal defects are rarely encountered after the age of forty. The prognosis appears definitely worse in patients with primum defects and in those with significant pulmonary hypertension.

The clinical and electrocardiographic findings for each of the defects under discussion are described in considerable detail. Left ventricular enlargement and left axis deviation constituted the most important evidence of a primum-type defect.

An analysis of the radiologic findings revealed a cardiothoracic ratio of 53 per cent or more in 25 cases. In general, patients with primum defects had larger hearts. Right atrial enlargement of greater or lesser degree was always present. Prominence of the main pulmonary artery and of the right and left major branches was a constant feature and tended to be of moderate degree. A true "hilar dance" was seldom detected on fluoroscopic examination and the authors dismiss this sign as of little importance. Pulmonary plethora was not a notable feature in the majority of cases. The striking attenuation of peripheral pulmonary arteries characteristic of pulmonary hypertension was noted in only 8 patients in the present series. Pulmonary "wedge angiography" showed a typical "leafless tree" appearance in these cases. Right ventricular enlargement, usually of moderate degree, was a fairly constant finding, becoming more marked in congestive heart failure.

Hemodynamic data for 28 cases are tabulated.

Seventeen of the 43 patients were subjected to surgery for closure of the septal defect, usually by the open-heart technic. Of the 13 survivors, a good result was obtained in all but 1. Surgical repair of secundum defect in patients without pulmonary hypertension or cardiac failure has an extremely low mortality but, once these two complications develop, the risks of surgery increase alarmingly. Therefore, "operation should be advised on diagnosis in uncomplicated secundum defects. There is no justification for awaiting the development of symptoms." The risks of surgery are significantly greater in primum defects, but the natural history of the condition is such as to warrant facing this higher risk.

Ten illustrations, including 7 roentgenograms; 4 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Impression of the Left Atrium on the Superior Vena Cava and Sinus of the Venae Cavae in Mitral Disease. G. F. Garusi. Acta radiol. 54: 265-272, October 1960. (Roentgen Institute of Bologna University, Italy)

An impression on the superior vena cava and the sinus of the venae cavae caused by the enlarged left atrium in cases of mitral disease is described. It is shown to bear a definite relationship to the degree and type of atrial enlargement as well as to the sagittal diameter of the thorax. The findings have been collected from routine angiocardiographic examinations. Serial films in two projections were obtained in all cases.

The direction of the enlargement of the left atrium is dependent upon the type of thorax. In the flat chest, the enlargement will occur mostly in transverse

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direction. The orientation of the heart and the thorax and the size of the other cardiac chambers are also among the factors which may influence direction of atrial expansion.

Another feature which is mentioned is a reflux into the arch of the azygos vein, present in varying degrees in 6 of the 9 cases studied. This sign, which the authors have observed in other heart conditions, might in these cases of mitral disease be interpreted as being caused by decreased blood flow in the superior vena cava; this may be due in part to the compression by the enlarged left atrium on the subazygotic tract of the superior vena cava, but mostly to the higher right endo-atrial pressure, further increased by the injection of contrast medium. Reflux may also be seen in the inferior vena cava. The amount of this reflux is variable and is not proportional either to the size of the impression of the left atrium or to the reflux into the azygos vein; it may perhaps depend upon whether the orientation of the axis represented by the two venae cavae is perpendicular.

Ten roentgenograms; 1 table.

THEODORE E. KEATS, M.D.
University of Missouri

Calcification of the Wall of the Left Atrium. J. Boeyens, R. Van Steenberge, and I. Billiet. *J. belge de radiol.* 43: 479-493, 1960. (In French) (Hôpital Civil d'Alost (Aalst), Belgium)

The authors present a case of massive calcification of the wall of the left atrium. They emphasize the necessity of a careful radiological examination to demonstrate these calcifications: multiple projections, high-kilovolt technic, tomography. They believe that atrial massive calcification is rare but that partial calcification is much more frequent.

Calcification of the wall of the left atrium is always of rheumatic origin and is usually found in a mural thrombus or in the endothelium; calcification of the mitral valve and auricular fibrillation are always present. Mitral stenosis always predominates over other valvular lesions.

Six roentgenograms.

RENÉ HOURI, M.D.
New York, N. Y.

Probable Pericardial Cyst—Report of an Unusual Case. Richard A. Jones and William F. Bethard. *California Med.* 93: 39-42, July 1960. (7755 Fay Ave., La Jolla, Calif.)

A mesothelial cyst of the anterior inferior mediastinum, probably of pericardial origin, was suspected in a 36-year-old woman on palpation of a mass high in the epigastrium during deep breathing. Pneumoperitoneum was produced by the introduction of 300 ml of atmospheric air into the free peritoneal cavity. With the patient in the oblique position, a 3- to 4-cm. spherical lesion was demonstrated at the level of the diaphragm at its anterior insertion. At operation a tense, thin-walled cyst was removed intact from the mediastinum, including an adherent edge of thinned diaphragm. Microscopic examination showed the cyst to be lined with a single layer of mature mesothelial cells supported by loose areolar tissue.

Five illustrations, including 3 roentgenograms.

Critical Evaluation and Surgical Correction of Obstructions in the Branches of the Aortic Arch. Elliott S. Hurwitz, Charles A. Carton, Stanley C. Fell, Laibe

A. Kessler, Bernard Seidenberg, and Jerome H. Shapiro. *Ann. Surg.* 152: 472-484, September 1960. (Montefiore Hospital, New York, N. Y.)

A number of procedures are available for the correction of obstructions in the extracranial portion of the arteries supplying blood to the brain. At present, total cerebral angiography (intravenous or intra-arterial aortography and carotid arteriography) provides the surest guide to case selection for these procedures. Five cases are reported to illustrate some significant features of the general problem which, in the authors' opinion, have not received sufficient emphasis. These include the importance of total cerebral angiography; the occurrence of headache after correction of the obstruction; the buckled or kinked redundant internal carotid artery; the role of temporary shunts during the reconstructive maneuvers; and the future development of flow studies to supplement the clinical and radiologic data.

Endarterectomy or bypass procedures are most effective in patients with "small strokes," are infrequently of benefit in established strokes, and are to be avoided when intracranial vascular obstructions are present. The buckled or kinked internal carotid arteries may be obstructed just as effectively as those with internal blocking lesions, and are best treated by resection of the buckled segment and end-to-end anastomosis. Headaches following re-establishment of carotid arterial flow are self-limited and presumably on the basis of reactive hyperemia.

Ten roentgenograms; 16 drawings; 7 diagrams; 1 table.

GARTH R. DREWRY, M.D.
Tampa, Fla.

Diagnostic Value of Absence of the Physiologic Impression of the Aortic Arch on the Esophagus. A. Bigo and R. Dall'Acqua. *Radiol. med. (Milan)* 46: 537-550, June 1960. (In Italian) (Ospedale Mauriziano di Torino, Italy)

Failure of the aortic arch to make the normal impression upon the left side of the barium-filled esophagus is due to disturbance of the normal relationship between these two structures. The authors feel that lack of such impression is of diagnostic significance and consider many examples encountered first-hand. The impression is minimal or even absent in infancy, becoming deeper with the passing years. It is usually less in the female because of the smaller caliber of the aortic arch.

The various anomalies of the aortic arch are prominent among the causes of disturbance of the physiologic impression produced upon the esophagus. With anomalous origin of the right subclavian artery (arteria lusoria), the posterior impression and displacement of the esophagus forward and to the right render the usual impression of arch upon esophagus less marked, or it may even be absent. Dextroposition of the aortic arch, double aortic arch, right-sided aortic arch with posterior diverticulum, all have their effect on the normal impression. In coarctation of the aorta, the sub-aortic segment of the esophagus is displaced anteriorly and to the right by the post-stenotic dilatation of the descending aorta. This minimizes the normal impression of the arch upon the esophagus, while the dilated poststenotic segment causes an impression upon the esophagus deeper and lower than normal.

Extensive aneurysms may displace the esophagus to the right and posterior, or to the right and anterior, with an increased impression. However, when the

ascending arch is involved, the aortic arch may be displaced to the left, minimizing the impression.

An enlarged pulmonary artery, either acquired or congenital, might displace the esophagus to the right and posteriorly, with loss of the normal impression.

An uncoiled aortic arch from sclerosis may cause a partial separation of esophagus and arch with diminished impression.

In mitral heart disease with enlargement of the left atrium, the esophagus may be displaced, thus making the impression less. The hypoplastic aortic arch may be another factor, as may rotation of the heart.

Thyroid enlargements may minimize the physiologic impression by either posterior displacement of the esophagus *via* the bronchus, or displacement of the aortic arch. Similar effects may be exerted by any abnormal tissue masses in the mediastinum, congenital, neoplastic, or inflammatory.

The esophago-aortic relationships may be disturbed in thoracic abnormalities, such as scoliosis and kyphosis. The aortic arch follows the curvature of the spine, to which it is more or less fixed by the intercostal arteries. The esophagus may either follow the arch or not in its displacement. In the latter case the aortic impression may be diminished.

A variety of pleuropulmonary processes, especially in the right upper lobe, such as scarring, atelectasis, tuberculosis, etc., may displace the esophagus to this side, with loss of normal aortic impression.

Twenty roentgenograms; 3 drawings.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Buckling and Kinking of the Carotid Vessels in the Neck. John A. Culligan. *Minnesota Med.* 48: 678-683, October 1960. (1135 Lowry Medical Arts Bldg., St. Paul 2, Minn.)

Buckling of the innominate-carotid arterial system and kinking of the internal carotid artery are discussed. Differences in etiology, clinical implications, and treatment in the two conditions are outlined and contrasted.

The diagnosis of buckling may be made if the possibility of its presence is kept in mind. Characteristically, the postero-anterior chest roentgenogram provides a clue in that the aortic arch rides higher than normal, often presenting at or above the level of the clavicles. The author has used forward angiocardiology to good advantage in the delineation of the lesion. Fifty to 80 c.c. of 90 per cent sodium diatrizoate (Hypaque) or 85 per cent methylglucamine diatrizoate (Cardiografin) is employed in conjunction with a Schönander rapid cassette changer. Single film technic is adequate if the circulation time from the basilic vein can first be determined with a tracer dose of radioactive albumin.

Diagnosis of kinking of the internal carotid rests upon angiographic visualization of the carotid system. Although direct percutaneous carotid puncture is often employed, the author believes that mapping of the entire carotid system is preferable. This may be accomplished by retrograde aortic catheterization by way of the femoral artery, or by direct puncture of the aortic arch *via* the right supraclavicular approach. In this way, both carotid arteries are demonstrated in their entirety, as well as the vertebral arteries, and proximal carotid or innominate occlusion (pulseless disease) will not be overlooked.

Three roentgenograms; 3 drawings.

Haemangiopericytoma: Angiographic Findings. N. Joffe. *Brit. J. Radiol.* 33: 614-617, October 1960. (Baragwanath Hospital, Johannesburg, Union of South Africa)

The author reports a case of hemangioma of the thigh, with particular attention to the angiographic findings. The patient, a 42-year-old African male, was admitted to the hospital with a swelling on the lower half of the left thigh which had originally appeared six years previously. The mass had been excised but recurred after a short interval and had gradually increased in size. Fifteen cubic centimeters of 60 per cent Urografin was injected percutaneously into the left femoral artery. The arterial phase of the examination showed slight medial displacement of the distal portion of the femoral artery; numerous but normal-appearing small arterial twigs were noted in the region of the soft-tissue mass. The capillary and venous phases revealed a persistent uniform contrast "blush," outlining the mass, pathological vessels at the lower pole of the tumor, large draining veins at the proximal pole, and veins running at right angles to the normal flow of venous blood on the inner aspect of the mass. The angiographic findings were not specific for hemangiopericytoma apart from indicating a vascular soft-tissue tumor. Certain features (evidence of a pathological circulation and veins coursing at right angles to the normal flow of venous blood) favored a malignant growth. Microscopic examination disclosed a malignant hemangiopericytoma.

A search of the literature revealed only one other case of hemangiopericytoma in which the angiographic findings are illustrated (Reynolds and Lansche: *J. Bone & Joint Surg.* 40-A: 921, 1958). In this case arteriography revealed the presence of numerous small vessels forming a rich vascular network, the picture differing somewhat from that obtained in the author's case.

Three roentgenograms; 3 photomicrographs.

HAROLD A. SWANSON, M.D.
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THE DIGESTIVE SYSTEM

Respiratory Kymography in Acute Abdominal Conditions. Sam Schmidt. *Acta radiol.* 54: 49-68, July 1960. (Karolinska Sjukhuset, Stockholm, Sweden)

The author describes the technic of respiratory kymography employed at the Karolinska Sjukhuset, Stockholm. The procedure has been carried out in 500 patients, 87 of whom had acute abdominal conditions. The present report is based on these 87 cases and 30 normal control subjects.

In each examination, two films were exposed, one during ordinary respiration and the other during deep breathing. Patients were examined in the supine position, with the x-ray tube below the table, to eliminate body movements during respiration.

The tracing of the normal diaphragmatic movements consisted of a number of asymmetric steep waves. The ascending, expiratory limb was straight in its lower two-thirds and slightly curved in its upper third, indicating some slowing down toward the end of expiration. The descending, inspiratory limb formed a straight line. The apex of the wave was a sharp-pointed angle. The rib movements were opposite in direction to the diaphragmatic excursions. In general, the wave was slightly undulating, but in some cases the transition be-

tween inspiration and expiration was a pointed angle. The diaphragmatic and costal movements were synchronous and similar on both sides in respect to configuration, amplitude, and frequency of waves. There was, however, a slight difference in amplitude between the two sides in diaphragmatic movements and to an even greater degree in the costal movements.

In the majority of patients who had either a subphrenic abscess, multiple liver abscesses, severe postoperative abdominal hemorrhage, acute cholecystitis, or acute pancreatitis, the common finding was a plateau-shaped diaphragmatic wave. As a rule, it was present on the affected side only. In the cases of ileus, it was present on both sides. No plateau wave was found in cases of visceral perforation; this seems contradictory, and further investigations are being carried out. The plateau wave represents a short apneic period at the end of expiration.

The diaphragmatic amplitude was reduced in all but 6 of the patients with severe abdominal disorders, and the degree of restriction always more marked on the affected side in localized conditions. This was true in about half of the cases of abdominal pain of unknown origin. Diaphragmatic paralysis was relatively rare, being found only in 2 cases of subphrenic abscess and in 1 of ileus.

The author discusses the sources of error in the interpretation of the kymograms. He concludes that kymography often makes it possible to distinguish abdominal from intrathoracic conditions and to localize the process to the right or left side of the abdomen. It will also aid in differentiating severe intra-abdominal conditions from those that are less acute.

Seventeen figures. GEORGE C. BARRETT, M.D.
Bowman Gray School of Medicine

Roentgen Features of the Normal and Herniated Esophagogastric Region. Problems in Terminology. Bernard S. Wolf. *Am. J. Digest. Dis.* 5: 751-769, September 1960. (Mount Sinai Hospital, New York 29, N. Y.)

The identification of a sliding hiatal hernia must be based on the demonstration of a pouch of stomach above the hiatus of the diaphragm. The problem of fulfilling the diagnostic criteria in cases of minimal herniation may be considerable. When coated with thick barium, the esophagogastric region is collapsed and the esophageal folds may be as thick and tortuous as gastric rugae. During distention with fluid barium, however, the folds in the esophagus are effaced, while gastric rugae within the hernial sac often persist.

When the esophagus is uniformly distended throughout its extent, a moderate increase in caliber normally occurs above the diaphragm. This rather diffuse dilatation, with no clearcut proximal demarcation, has been termed the "phrenic ampulla" and is responsible for the "phrenic ampulla phenomenon" due to trapping of ingested barium in the distal esophagus between the advancing peristaltic wave and the pinch cock action at the diaphragm. As a result, a sac of variable and continuously decreasing height is produced immediately above the diaphragm. The apex of this sac represents the stripping peristaltic contraction, which moves distally at a low rate because of resistance at the level of the diaphragm. If this resistance is overcome, the barium will enter the stomach as the sac above the diaphragm diminishes. If resistance is maintained, the peristaltic contraction at the apex of the sac may

be forced to relax and barium will then reflux proximally into the esophagus. With successive peristaltic waves and repeated reflux, there remains eventually a small sac filled with barium for a considerable period, and it is this that the author would call the true phrenic ampulla.

Lerche has designated the junction of the tubular esophagus and the phrenic ampulla as the "inferior esophageal sphincter." Under normal circumstances, however, true sphincteric activity localized to this region is not evident.

The best criterion available to indicate the level of the esophageal hiatus is the abrupt diminution in the distensibility of the lumen at the hiatus that is regularly seen if the film is obtained while the patient is drinking fluid barium rapidly. This narrow channel measures about 2 cm. in length and corresponds to the point of respiratory reversal seen on intraluminal pressure curves. The esophagogastric epithelial junction lies somewhere within this channel. The designation abdominal esophagus is thus not wholly appropriate for this segment, and it has been designated the "submerged segment" or the "abdominal gullet."

The level of the hiatus, that is, the beginning of the abdominal gullet or submerged segment, can ordinarily be demonstrated without special maneuvers. If there should be any question, the pinchcock action at the diaphragm can be used to exaggerate the difference in caliber of this segment from the remainder of the esophagus above the hiatus. Under normal circumstances, therefore, there are three main divisions of the tube extending from the pharynx to the stomach: (1) the tubular esophagus, (2) the phrenic ampulla, (3) the submerged segment. The submerged segment may be subdivided into an intrahiatal and infrahiatal portion.

When the esophagogastric epithelial junction is displaced above the hiatus, a new feature appears in many instances, namely, a ring or shallow web or circumferential diaphragm evident when this region is maximally distended. It is seen on roentgen examination as a lucent transverse band 2 or 3 mm. in width traversing the barium column from side to side and manifested in profile by sharply demarcated, somewhat rectangular or angular notches. This ring was described by Templeton as part of the phrenic ampulla phenomenon. It appears to be the ring described by Schatzki and Gary (*Am. J. Roentgenol.* 70: 911, 1953. *Abst. in Radiology* 63: 601, 1954) and Ingelfinger and Kramer (*Gastroenterology* 23: 419, 1953. *Abst. in Radiology* 62: 135, 1954). It has been shown at autopsy and surgical biopsy that the esophagogastric mucosal junction was located at the site of this ring. While the nature and origin of such an epithelial junctional ring is essentially unknown, it is of interest in that it constitutes a most useful roentgen finding, permitting recognition of small hernias in many patients.

The term "vestibule" has been applied to the segment of the esophagus between the inferior esophageal sphincter and the epithelial ring. Under normal circumstances—that is, in the absence of a hernia—it must extend from the inferior esophageal sphincter (located 1 or 2 cm. above the hiatus) to the epithelial junction, 1 or 2 cm. below the hiatus. The normal phrenic ampulla represents the supraliatal portion of the vestibule. The abdominal portion of the vestibule corresponds to the proximal part of the submerged segment. Normally, the vestibule as a single distensible region is not apparent.

It has been demonstrated by intraluminal pressure studies that the terminal portion of the esophagus over a distance of about 3 to 4 cm. has unique functional characteristics that resemble sphincteric action, both under normal circumstances and in patients with hiatus hernia. The location of this "high-pressure zone" corresponds approximately to the vestibule, as described above, and the sphincteric region has been referred to as the vestibule.

The interested reader is urged to study this paper, with its excellent diagrams, in the original.

JOHN P. FOTOPOULOS, M.D.
Northwestern University Medical School

The Diagnoses in 100 Cases with Roentgenographic Defects of the Gastric Antrum. Charles M. Thompson, Leonard S. Dreifus, and Harold Heintz. *Am. J. M. Sc.* 240: 291-307, September 1960. (Philadelphia General Hospital, Philadelphia 4, Penna.)

All cases at Philadelphia General Hospital in which a roentgenographic abnormality of the gastric antrum was reported between November 1949 and April 1954 were reviewed. Those in which a final diagnosis was established by tissue examination (99 cases) or by operative inspection (1 case) were submitted to further analysis. The roentgen diagnoses in these 100 cases were carcinoma of the antrum, 55 cases; benign ulcer of antrum, 22; extrinsic defect of antrum, 10; gastritis of antrum, 6; "pyloric obstruction," 6; carcinoma of pancreas, 1. The histologic diagnoses were carcinoma of antrum, 43; benign ulcer of antrum, 31; gastritis of antrum, 11; carcinoma of pancreas, 3; pancreatic rest of antrum, 1; tuberculosis or sarcoidosis, 3; prolapsed gastric mucosa with gastritis, 1; reticulum-cell sarcoma, 1; carcinoma of gallbladder, 1; carcinoma of urinary bladder, 1; no pathology, 4.

In no instance did the roentgenologist fail to predict malignancy when malignancy was present. Usually he was reluctant to discard the possibility of cancer if any one of the following findings was demonstrated: distortion of the mucosal pattern, marginal subtraction defects, unusual rigidity or lack of distensibility of the area, and space-filling defects. This conservatism had the effect of increasing the number of predicted malignant lesions. Symptoms and physical findings, with the exception of a palpable mass, which proved to be malignant in all but 1 case, were not specific for a type of disease and did not differ in benign and malignant lesions.

Eleven illustrative cases are reported. In an unusual case tuberculosis of the antrum simulated tumor.

Eleven roentgenograms; 1 diagram; 5 tables.

GARTH R. DREWRY, M.D.
Tampa, Fla.

Factors in the Radiological Differential Diagnosis of Pyloric Ulcer. 1. **The Pyloric Orifice Simulating an Ulcer.** A. D. Keet, Jr., and J. J. Heydenrych. *South African M. J.* 34: 881-882, Oct. 15, 1960. (Karl Bremer Hospital, Bellville, Union of South Africa)

2. **A Common Normal Prepyloric Mucosal Furrow Simulating an Ulcer.** A. D. Keet, Jr. *South African M. J.* 34: 882-884, Oct. 15, 1960.

In practice the radiological diagnosis of an active gastric ulcer depends on the demonstration of an ulcer cavity. This may have the appearance of (a) a barium-containing projection from the lumen, in which case the ulcer is seen in profile on one of the margins of the organ,

or (b) a persistent dense fleck. Here the barium-containing ulcer cavity is seen end-on. In these papers two conditions often mistaken for ulceration or tumor are described.

In the first paper, 3 cases are presented in which a constant dense fleck of barium in the pyloric orifice, surrounded by a radiolucent zone and radiating mucosal folds, resembled an ulcer at the pyloroduodenal junction. In all 3 instances the stomach and duodenum were proved free of ulceration and tumor, but because of the peculiar direction of the pyloroduodenal axis and moderate spasticity of the prepyloric area, the caudal end of the latter was projected over the base of the duodenal bulb and could not be separated from it. Consequently, the pyloric orifice was seen end-on and presented as a constant fleck. In 2 of the cases there were massive adhesions between stomach, liver, and duodenum.

In the second paper, an example is given of a small, ulcer-like projection on the lesser curvature of the prepyloric area of the stomach, which was found to represent an oblique prepyloric mucosal fold, with an accompanying mucosal furrow on its caudal side. This is a common observation in the normal stomach when the canalis egestorius is relaxed or partially contracted. The barium-containing mucosal furrow may present as a niche on the lesser-curvature side. When the canalis contracts maximally, the fold and furrow change in direction and come to lie longitudinally, and the "niche" disappears.

Ten roentgenograms.

Clinical Importance of Gastric Varices. Samuel Kark and George T. Wohl. *New England J. Med.* 263: 665-669, Oct. 6, 1960. (G. T. W., Temple University School of Medicine, Philadelphia, Penna.)

Gastric varices are being seen increasingly often in patients with acute gastrointestinal hemorrhage. This increased frequency is associated with a greater number of cirrhotic patients encountered in hospital practice. Although gastric varices occur predominantly in the cardiac end of the stomach, they may be found along the lesser curvature and throughout the fundus. They usually appear as smooth, rounded masses, 1 to 2 cm. in diameter, projecting into the gastric lumen. While the roentgen picture is often characteristic, it may mimic other entities, prominent among which are cancer of the cardiac end of the stomach and hypertrophy of the mucosal folds. Demonstration of the portal collateral circulation may be accomplished by splenoportography; during this procedure the portal pressure can also be obtained.

Fifteen cases with a clinical and laboratory diagnosis of Laennec's cirrhosis were reviewed. A gastrointestinal series, including an esophagram, had been obtained in each; in 7 there was no evidence of gastric or esophageal varices on these studies. In 6 of the 7, however, gastric varices were demonstrated by splenoportography, in 1 the varices were large and numerous. In 2 the veins of the fundic plexus carried contrast medium in a retrograde direction, although they did not appear to be dilated. In 4 cases in which gastric varices were diagnosed roentgenographically, their presence was confirmed by splenoportography. In 2 cases esophageal varices were seen on the roentgenogram and both gastric and esophageal varices were noted on splenoportography. Splenoportography was unsuccessful in 3 of the 15 cases.

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Four cases are reported in 3 of which the preoperative diagnosis, based chiefly upon the x-ray findings, was carcinoma of the cardiac end of the stomach. Varicosities were found at surgery. In the fourth case the index of diagnostic suspicion regarding gastric varices was considerably higher, and after the x-ray demonstration of a mass in the cardiac end of the stomach, splenoportography was performed. This showed the mass to represent an unusually large group of dilated veins at the esophagogastric junction.

Attention is called to the frequent occurrence of gastric varices in patients with portal hypertension. The anatomy of the portal venous system is described, and the changes which take place when the portal pressure becomes increased are summarized.

Three roentgenograms; 1 diagram; 1 table.

D. I. COPE, M.D.

Mercy Hospital, Pittsburgh, Penna.

Regional Enteritis in Children. John E. Moseley, Richard H. Marshak, and Bernard S. Wolf. *Am. J. Roentgenol.* 84: 532-539, September 1960. (The Mount Sinai Hospital, New York, N. Y.)

The early diagnosis of regional enteritis in childhood requires an awareness of the substantial incidence of the condition in children, particularly in the group between ten and fifteen years of age. The authors report a study of 28 cases seen between the ages of seven and fifteen. In 20 cases the distal ileum was involved, in 4 both the ileum and colon, and in 4 the ileum and jejunum. The roentgen findings were essentially similar to those described in adults (see, for example, Marshak and Wolf; *Am. J. Roentgenol.* 74: 1000, 1955. *Abst. in Radiology* 67: 619, 1956).

The early symptoms of regional enteritis in children are frequently vague and misleading. All of the cases in the present series fell into one of the three following categories; (1) those operated on for acute appendicitis or explored with that probability in mind; (2) those presenting mild symptomatology not suggestive of regional enteritis; (3) those with abdominal cramps and diarrhea, eventually of such an intensity as to suggest intestinal inflammatory disease.

A significant number of cases of acute ileitis in children go on to spontaneous recovery and apparently do not progress to a chronic stage. In others, the chronic form of granulomatous ileitis is seen. In this latter group, a careful interrogation of the patient or the parents will disclose a history of previous mild abdominal distress, diarrhea, fever, or anorectal fistulas. The relationship, if any, between nonrecurrent, nonsclerosing ileitis and the chronic granulomatous form of enteritis is still undetermined. Twenty-three of the 28 cases were of the nonstenotic variety, reflecting the relatively short duration of the disease. Despite repeated roentgen examinations over a period of many years, no proximal and distal extension of the disease process was observed.

Ten roentgenograms; 2 tables.

ROBERT L. EGAN, M.D.

University of Texas, Houston

Extra-Abdominal Abscesses of Intestinal Origin.

J. G. Duncan and Eric Samuel. *Brit. J. Radiol.* 33: 627-630, October 1960. (Royal Infirmary, Edinburgh, Scotland)

Extraperitoneal abscesses arising from the alimentary canal usually remain localized to the adjoining soft

tissues. They may, however, extend into the inguinal and femoral regions, and considerable difficulty may be experienced in their diagnosis. The use of antibiotics in abdominal infections has so modified the clinical course of inflammatory processes that large intra-abdominal abscesses may develop with little or no constitutional disturbance. This is equally true of extraperitoneal abscess formation and intraperitoneal suppuration. Such an abscess may track widely and insidiously and may present in sites remote from the original lesion. Extraperitoneal abscesses on the right usually follow infections of the cecum or terminal ileum, of which Crohn's disease appears to be the most common: on the left side, infection usually follows diverticulitis of the pelvic colon.

The radiologic findings in extra-abdominal abscesses are similar to those of abscesses in other sites, but certain features may suggest the intestinal origin. As in other abscesses, a soft-tissue swelling with blurring of intermuscular planes will be noted with the formation of a homogeneous mass: the continuity of this swelling with the site of origin of the abscess may be demonstrated. The presence of gas in the abscess is suggestive of an intestinal origin; this may be due to direct escape of gas from the bowel or to gas-forming organisms. The gas may appear as numerous small bubbles in the subcutaneous tissues and intermuscular planes or be aggregated into larger bubbles. The demonstration of gas in the subcutaneous tissues and muscle planes and its absence in the muscles largely rules out gas gangrene. Occasionally fecal material may be seen within the abscess, making the diagnosis obvious.

Three cases with almost identical radiological findings are reported. The extent of the abscess presenting in the thigh was demonstrated very accurately. Two of the abscesses occurred on the left and were due to carcinoma of the colon. The underlying cause of the one on the right side was Crohn's disease of the terminal ileum.

Three roentgenograms.

HAROLD A. SWANSON, M.D.

Calgary General Hospital, Calgary, Alta.

Fistula Formation Between the Duodenum and Colon. A Report of Three Cases and a Review of the Condition. D. G. Calvert and G. A. Medhurst. *Brit. J. Surg.* 48: 136-139, September 1960. (Westminster Children's Hospital, London, England)

Most duodenocolic fistulas have a malignant origin, the majority being due to a carcinoma of the right colon. Two of the 3 cases of duodenocolic fistula which the authors report were the result of carcinoma of the hepatic flexure region. In the third, the fistula was a complication of gallbladder cancer, with massive involvement of the adjacent viscera.

The symptoms of fistula between the duodenum and colon are basically those of the underlying condition, with the characteristic results of fistula formation superimposed. It is generally held that examination by barium enema is superior to the barium meal for demonstrating the fistulas, but the authors found the opposite to be true. In the first case the fistula was shown clearly by barium meal and, owing to the patient's frail condition, further studies were not carried out. In the second case, the fistula was visualized by both barium meal and by barium enema. In the third, the barium-enema examination failed to show the fis-

tula which was well demonstrated following a barium meal.

The treatment of fistulas due to a primary malignant neoplasm, usually of the colon, is essentially treatment of the tumor. Laparotomy was performed in all of the authors' cases, and successful resection was carried out in 2. In the last case the spread was too extensive for resection to be attempted.

Three roentgenograms; 1 photograph in color.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

Parietography of the Large Intestine. G. C. Canossi, M. Dardari, and A. Santino. *Radiol. med. (Milan)* **46**: 631-648, July 1960. (In Italian) (Istituto di radiologia dell'Università di Modena, Italy)

Parietography of the large intestine is the radiologic study of the wall of the large intestine by means of simultaneous endo- and exovisceral gaseous insufflation. In the case of the rectum, the gas is introduced retroperitoneally. Stratigraphy is an integral part of the method. Similar study of the wall of the stomach and bladder has proved its worth, and the present technic is merely an extension from these older studies.

The method affords a precise definition of gross morphology, giving practically a complete anatomic reconstruction. It permits confirmation or rejection of a diagnosis of neoplasm suspected from the preliminary studies (which, incidentally, must always be performed); it may show the tumor to be much larger than was suggested by routine examinations; it may demonstrate hepatic, peritoneal, or nodal metastases; it may allow a differentiation between malignancy and benignancy.

Technical difficulties are minimal and the procedure is without danger.

Thirty-four roentgenograms.

CHRISTIAN V. CIMMINO, M.D.

Fredericksburg, Va.

Efficacy of Double Contrast Method in Radiologic Diagnosis of the Colon. A. Rüttimann. *Schweiz. med. Wchschr.* **90**: 807-812, July 23, 1960. (In German) (Zentraldiagnostische Röntgeninstitut der Universität Zürich, Switzerland)

The diagnostic accuracy of double-contrast roentgen examination of the colon by Welin's technic with Barostat as a contrast medium in investigation of the colon is demonstrated. Careful preparation of the patient is emphasized, including residue-free diet the day before, castor oil, and thorough cleansing enemas. A colloidal type of barium is preferred because of the type of coating on the mucous membrane. The advantage of the double-contrast method is most notable in the detection of polypoid lesions. Sixteen excellent roentgenograms are reproduced.

CHARLES M. NICE, JR., M.D., PH.D.

Tulane University

Pseudopolyps of the Cecum from Inverted Appendiceal Stumps. Terrence J. Murphy, Leonard G. Powsner, and James F. Regan. *West. J. Surg.* **68**: 306-308, September-October 1960. (T. J. M., Shaughnessy Hospital, Vancouver, B. C., Canada)

Three cases of pseudopolyp of the cecum due to an inverted appendiceal stump are reported. Although no specific symptom complex has been ascribed to this

condition, it is important because in some instances it cannot be distinguished from a neoplasm. All 3 of the authors' patients were young women with vague low abdominal or right lower quadrant symptoms and minor disturbances. It is felt that these symptoms were not necessarily related to the harmless pseudopolyp removed at surgery.

In only one of the cases were the radiographic studies diagnostic. In that instance the pseudopolyp presented as a small, rounded, discrete filling defect at the tip of the cecum, protruding into the lumen as a sessile polyp on double-contrast examination.

All 3 patients were operated upon, and in all the postoperative course was uneventful. The 3 surgical specimens were nearly identical in size and in their gross and microscopic appearance. In each case a relatively normal but thin cecal mucosa covered the inverted appendiceal stump; the muscularis of the stump was well preserved.

Experiments performed on specimens of the cecum and appendix from cadavers showed that the size of the pseudopolyp is directly related to the diameter of the purse-string suture. The number of recorded cases of pseudopolyp of the cecum is too small to warrant condemnation of inversion of the stump on this basis alone.

Surgery is indicated when a small cecal filling defect is present in the roentgenogram, since neoplasm cannot be ruled out by any other means. Awareness of the condition may help to avert a bowel resection for a benign lesion.

Two roentgenograms; 1 photograph; 2 photographs.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Appendicular Calculi. B. R. Meyerowitz. *Brit. J. Radiol.* **33**: 631-633, October 1960. (Hammersmith Hospital, London, W. 12, England)

Appendiceal calculi (coproliths, fecaliths) are observed most often in young persons. The author, however, reports a case in a 53-year-old man who was seen in the emergency department of the hospital with hypogastric pain and vomiting. Roentgen examination on two occasions ten to fifteen years previously had revealed a duodenal deformity but no actual ulcer. A roentgenogram of the abdomen was obtained and was interpreted as showing no abnormality. Three days later the patient was readmitted to the hospital with severe pain, and a diagnosis of perforated duodenal ulcer was made. Surgery disclosed a ruptured appendix with a large calculus at the site of the rupture. Retrospectively, the initial abdominal roentgenogram showed a large lamellated calculus in the right iliac fossa, which could have been recognized as an appendiceal calculus from its pattern of calcification and its location.

Attention is called to the characteristic lamellated appearance of appendiceal calculi and to the high incidence of associated acute appendicitis and perforation of the appendix. Calcified mesenteric nodes are distinguished by their mottled appearance: ureteric calculi lie in the axis of the ureter, and gallstones are not usually so low. If the patient is not acutely ill, cholecystography and intravenous pyelography may be useful in the differential diagnosis.

One roentgenogram; 2 photographs.

HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

Chronic Follicular Cholecystitis. Radiological, Pathological and Surgical Aspects. R. L. Estrada, N. M. Brown, and C. E. James. *Brit. J. Surg.* **48**: 205-209, September 1960. (Montreal General Hospital, Montreal, Quebec, Canada)

Chronic follicular cholecystitis is a rare chronic gallbladder inflammation characterized by formation of lymph follicles with hyperplastic germinal centers in all layers of the gallbladder. In the gross specimen, these appear as round prominences of firm consistency elevated above the inner surface of the organ. The condition is frequently seen in association with typhoid fever; in other instances the etiologic agent may remain undetermined.

In a review of 2,473 gallbladders removed surgically, the authors found only 2 cases of this type.

The preoperative diagnosis is difficult but may be suspected in a patient with gallbladder symptoms and typhoid fever history. The symptomatology is that of chronic cholecystitis with or without biliary calculi. Cholecystography may reveal the diagnosis but differentiation from multiple papillomata and cholesterosis is necessary. In cholesterosis, the shadow is often unusually dense and the gallbladder contracts unusually well in response to a fat meal. The cholesterol masses which adhere to the mucosa cause translucent irregular shadows in radiographs and do not move with change in the patient's position. In cholelithiasis, similar small radiolucencies may be seen, but usually change position with compression or variation of the patient's position. The defects of multiple papillomata should not change position, but the gallbladder should concentrate well.

In the absence of biliary calculi, the key point in the diagnosis of chronic follicular cholecystitis appears to be a gallbladder showing a faint shadow because of impaired function: numerous small round translucencies casting a ragged irregular outline in the cholecystogram; and the fact that this appearance does not change as the patient is re-positioned. Probably the disease could be so far advanced as to cause non-function, either by blockage by the giant lymph follicles at the origin of the cystic duct or by compression of an enlarged cystic lymph node.

Since chronic follicular cholecystitis may not be differentiated from multiple papillomata, cholecystectomy is recommended. In either case, an infected gallbladder may be removed and/or the possibility of malignant change in the papilloma is eliminated. If the condition is due to typhoid fever, cholecystectomy and choledochostomy with T-tube drainage might remove the source of chronic infectivity.

Two roentgenograms; 4 photomicrographs; 2 color photographs.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

Radiological Aspects of Cholo-Enteric Fistulae. James G. Snead. *Virginia M. Monthly* **87**: 571-573, October 1960. (30 Franklin Rd., Roanoke, Va.)

Internal biliary fistulas are not common. They are usually caused by a biliary calculus perforating into the adjacent structures. The first preoperative radiological diagnosis of internal biliary fistula was made in 1915. Prior to 1941 only 90 cases had been diagnosed radiologically, but by 1951 this number had increased to 181.

Positive roentgen criteria include the demonstration of the fistula either by gas in the biliary system or perhaps by barium passing into the ducts during either a

gastrointestinal series or a barium-enema examination. The gallbladder may not be visualized. Air may be seen on a preliminary film of the abdomen or gallbladder area, either outlining the major biliary ducts or, more frequently, only small segments of the ductal system. Demonstration of air in the hepatic ducts is almost pathognomonic of fistula. Rarely, in emphysematous cholecystitis, gas may be noted within the gallbladder but its presence in the biliary ducts in that condition is unusual.

The author reports 3 cases of cholo-enteric fistula—one choledochoduodenal, one cholecystoduodenal, and one cholecystocolic: all were diagnosed preoperatively.

Four roentgenograms.

WILLIAM H. ELLSWOOD, M.D.

Charleston, W. Va.

Lime-Water Bile. Bernard Nolan, James A. Ross, and Eric Samuel. *Brit. J. Surg.* **48**: 201-204, September 1960. (Royal Infirmary, Edinburgh, Scotland)

Lime-water bile or "milk of calcium bile" is due to the formation of a suspension of crystals of calcium salts in the gallbladder, rendering the contained bile opaque to the x-ray. The authors found only 58 recorded cases, to which they add 3. Unless a preliminary film is made prior to ingestion of the contrast medium, however, the diagnosis may be missed. In only 3 of the previously reported cases was any of this lime-water bile seen in the duct system. In the authors' cases the ducts were also visualized.

The age and sex distribution for lime-water bile is the same as for other types of gallbladder disease. Obstruction at some point in the biliary tract appears to be a prerequisite. Obstruction of the cystic duct was present in all the reported cases in which the condition was limited to the gallbladder, and the common bile duct was obstructed in 6 cases including the authors'. If the obstructing stone moves into the common duct, then the ducts proximally may be opacified.

Chronic infection is stated to be essential, but there are many chronic cholecystitis cases without lime-water bile, so that another factor must be implicated. This does not appear to be an abnormality of calcium metabolism. It has been postulated that inflammation in the gallbladder produces a fall in cholesterol and bile salt content of the bile, leading to precipitation of calcium salts. Others have shown that, in the infected or inflamed gallbladder, the pH of the bile may remain alkaline instead of changing to acid as it does in the normal gallbladder. This would favor precipitation of calcium carbonate when the pH is above 6.6.

The finding of a pure suspension of calcium carbonate in the majority of reported cases suggests that rapid crystallization from a supersaturated solution has taken place. This may occur within a few days. If a preformed nucleus is present, precipitation about it will occur at a slower rate and form a stone.

Signs and symptoms of this condition are variable and simulate chronic gallbladder disease. If the obstruction is in the common duct, jaundice may be present.

The finding of an amorphous opacification of the gallbladder and/or ducts without the ingestion of contrast medium is diagnostic. In the erect position, the limey bile may layer out. One of the cases reported by the authors showed reflux of the bile into a pancreatic duct.

Four roentgenograms.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

Rapid Cholecystography. Samuel H. Madell and Milton Elkin. *Am. J. Digest. Dis.* 5:776-781, September 1960. (Albert Einstein College of Medicine, New York 61, N. Y.)

During early clinical evaluation of the cholecystographic medium, Orablix, it was observed that in some instances the gallbladder could be visualized very soon after oral ingestion of the opaque material. Since on occasion it would be advantageous to complete a roentgen examination of the gallbladder within three hours, a study was devised to evaluate three-hour cholecystography. One hundred and thirty-four patients were examined in the following manner:

Fasting patients were given 6 capsules of Orablix (0.75 gm. each) at 8 A.M., and at 11 A.M. a roentgenogram of the right upper quadrant was taken. If adequate opacification of the gallbladder had been achieved, routine cholecystography was performed, including post-contraction study after a fatty stimulus. If visualization was not adequate after three hours, the patient was instructed to maintain a fat-free diet for the remainder of the day, and return fasting the following morning, when a roentgenogram of the abdomen was obtained. If visualization of the gallbladder was satisfactory, routine cholecystography was carried out. If the gallbladder failed to visualize satisfactorily on the twenty-four-hour examination, the patient was given Telepaque (6 gm.) on the night of the second day, and the examination was repeated on the morning of the third day, twelve hours after Telepaque ingestion.

Visualization of the gallbladder was satisfactory after three hours in 39 patients (29 per cent). Only 71 of the remaining 95 patients were available for twenty-four-hour follow-up examination, at which time the gallbladder was adequately opacified in 38. The total number of examinations of diagnostic quality after twenty-four hours was therefore 77, i.e., 54 per cent of all patients or 70 per cent of those available for the complete study.

In 33 of the 110 patients available for the complete Orablix study, the gallbladder failed to opacify satisfactorily. Follow-up examination with Telepaque was carried out in 23 of these patients, and the gallbladder was visualized in 18.

One of the reasons for lack of success in achieving adequate visualization twenty-four hours after Orablix ingestion was failure of the patient to adhere to a diet free of fat.

The authors believe that, if rapid evaluation of the gallbladder status is desirable, Orablix ingestion may provide an answer at three hours. If visualization is inadequate at that time, one may either proceed with the intravenous examination or wait until the following morning for twenty-four-hour evaluation.

Seven roentgenograms: 3 tables.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

Emptying Effect on the Gallbladder of Tween 80. Lars Andrén and Georg Theander. *Acta radiol.* 54: 17-21, July 1960. (Malmö Allmänna Sjukhus, Malmö, Sweden)

The authors investigated the effect of Tween 80 (sorbitan mono-oleate) upon the emptying of gallbladders visualized with the sodium salt of iopanoic acid without concurrent demonstration of the bile ducts. At first Bilijodon capsules were employed which contained the sodium salt of iopanoic acid dissolved in a

mixture of Tween 80, polyethylene glycol (polyethylene oxide, Carbowax 400), and dipropylene glycol. In a significant number of cases these capsules produced visualization of the cystic and common ducts. Further experiments were then carried out, with capsules containing only one of the solvents. Polyethylene glycol and dipropylene glycol were found to have no appreciable effect on the size of the gallbladder. Tween 80 alone in a dosage of 0.15 gm. per kg., however, invariably caused the gallbladder to empty: in 8 out of 9 cases the bile ducts were visualized. With smaller doses the gallbladder contracted regularly though less markedly. The contraction of the gallbladder was first apparent at ten to thirty minutes, with the maximum at thirty minutes to two hours. No serious side-effects were encountered. The emptying effect of the Tween could be counteracted by oxicone-papaverine.

On the basis of these experiments, the authors conclude that Tween 80 may be used to advantage in the study of the evacuation capacity of the gallbladder and to demonstrate the bile ducts, provided sufficient contrast medium is present in the gallbladder. When given together with a contrast medium, as in Bilijodon capsules, it may possibly improve cholecystography in two ways, i.e., by accelerating the absorption of contrast medium and by emptying the gallbladder at a suitable moment.

Ten roentgenograms. JOSEPH E. WHITLEY, M.D.
Bowman Gray School of Medicine

Significance of Reflux of Contrast Material into the Hepatic Duct During Oral Cholecystography. C. Wieser and A. Neiger. *Schweiz. med. Wchnschr.* 90: 1083-1086, Sept. 24, 1960. (In German) (Rätisches Kantons- und Regionalspitals, Chur, Switzerland)

Although cholecystography was introduced in 1924, functional studies of the extrahepatic bile ducts have become possible only in the past fifteen years, with the aid of improved contrast materials. In addition, supine instead of prone views have helped to visualize bile ducts more distinctly and constantly. Even the hepatic duct and its branches can be seen quite frequently. Reflux into the latter is usually present in patients with postprandial pressure pain in the right upper quadrant.

Of a series of 738 patients, 102 had nonvisualization of the gallbladder. Cholelithiasis was suggested in 80 per cent. Calculi were found in 71 cases, including 11 in which they were seen on the preliminary roentgenogram. There was normal visualization in 336.

Either decreased or increased emptying time was observed in 169 patients. Reflux into the hepatic duct occurred 69 times, with associated postprandial pressure pain in 61 (88 per cent). In the majority of cases in this group the common duct was dilated (over 5 mm. wide). This was not attributable to the supine position, as it could also be seen with the patient erect. It was found that the dyskinesia was due either to cholecystitis and cholelithiasis or to disease of nearby organs.

It is emphasized that cholecystopathy without stones occurs much more often than cholelithiasis. All signs of functional disturbance must therefore be considered. In 226 cases with dyskinesia, reflux into the hepatic duct was seen 69 times, including only 9 cases of cholelithiasis. When the common duct was also dilated, an organic obstruction at the papilla of Vater had to be suspected.

Four roentgenograms. ERNEST KRAFT, M.D.
Northport, N.Y.

HERNIA

Two Cases of Omental Hernia of Morgagni, of Which One Was Associated with Hiatal Hernia. S. Panichi and I. Bonechi. *Radiol. med. (Milan)* 46: 449-455, May 1960. (In Italian) (Clinica medica generale dell'Università di Pisa, Italy)

With herniation of abdominal viscera through the foramen of Morgagni, symptoms are either lacking or non-specific. The radiologic diagnosis is easily made when the hernia contains a hollow viscus but difficult when it contains omentum. Plain studies show a rounded shadow in either anterior cardiophrenic angle, usually the right. This opacity is non-specific, and the differential diagnoses include all sorts of pulmonary, pleural, diaphragmatic, and mediastinal tumors, cysts, and malformations. A barium-enema study will show the mid-transverse colon drawn upward toward the herniated mass in the shape of a reverse V, especially when the patient is upright and in deep inspiration. This is not pathognomonic, however, since adhesions can produce the same picture. Pneumoperitoneum allows a definite diagnosis by demonstrating gas contained within the fine border of the abnormal cardiophrenic shadow, but even this procedure may fail if the neck of the hernia is obliterated by adhesions.

The first of the authors' 2 patients had an associated hiatal hernia, a very unusual occurrence. The barium enema demonstrated the reversed V sign, and gas was demonstrated within the right cardiophrenic shadow after pneumoperitoneum. The second patient, also with a right cardiophrenic shadow, had a normal transverse colon and no gas was apparent within the mass after pneumoperitoneum. The diagnosis was made at operation.

Ten roentgenograms.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

THE MUSCULOSKELETAL SYSTEM

The Radiographic Density of Avascular Bone. W. P. Bobechko and W. Robert Harris. *J. Bone & Joint Surg.* 42-B: 626-632, August 1960. (27 Bannockburn Ave., Toronto, Ont., Canada)

The increased radiographic density of avascular bone is traditionally described as only apparent, being secondary to hyperemic decalcification of the adjacent viable bone. The assumption is that the avascularity of the dead fragment prevents it from either gaining or losing calcium and hence that its density to x-rays must remain unchanged. A careful study of radiographs in most cases of avascular necrosis has shown, however, that the "dead" bone undergoes an absolute increase in density so that it becomes denser than the surrounding bone as well as denser than it was originally. Thus, it appears that this bone is in fact not dead but is actually undergoing reossification by the apposition of new bone on the surfaces of the unabsorbed dead trabeculae. If one assumes that the dead trabeculae do not lose calcium and that the new bone is normally calcified, then it seems logical to conclude that the increase in density observed radiographically is actually due to the process of reossification adding to the bulk of bone to be penetrated by the x-rays.

Experimental avascular necrosis of the femoral head was produced in rabbits and the histologic and radiographic changes were compared. During the first ten

days, x-ray examination revealed no change in the density of the femoral heads. Then increased density was seen in the distal part of the femoral neck, advancing toward the fracture line. This coincided with the first appearance of callus in the neck. After three or more weeks, the heads themselves showed increasing density, and by eight weeks almost every head exhibited this change. The density was absolute, being greater than that of the adjacent uninvolved bone, the control head, or of the involved bone itself at the beginning of the experiment. Histologically, there was a progressive ingrowth of new bone from the living distal fragment of the neck into the avascular head without absorption of the necrotic trabeculae. This ingrowth occurred slightly in advance of the appearance of the absolute increase in radiographic density in the early stages but coincided closely with the amount and position of newly formed bone.

It is concluded that the increased density to x-rays is the result of increased bone bulk, and that the radiographic density does not represent increasing necrosis but rather an increasing reossification of the involved area.

The authors were impressed by the rapidity with which new bone invaded the necrotic head. Within six weeks appositional new bone was found on the subarticular trabeculae, and in many instances the marrow spaces were almost obliterated by new bone. Where remnants of the epiphyseal plates persisted, they acted as a barrier to the ingrowth of new bone and temporarily halted the process. Absorption of dead bone was slow and was not observed in any detail during the eight-week span of the experiment. Since it is known that absorption of dead bone can occur only from a free surface, it seems likely that some of the necrotic fragments which are completely encapsulated by new bone may never be completely absorbed, or absorbed so slowly that increased radiographic density may persist for a long time. Phemister's term "creeping substitution," presumably coined to describe this type of histologic change, is considered misleading because it suggests that absorption of dead bone either precedes or coincides with the laying down of new bone. The authors' experience suggests that the phenomenon proceeds in two distinct stages; first, the rapid encapsulation of dead bone by new bone; second, the slow absorption of the dead material. The second stage may never be completed.

Whereas the avascular fragment may be rapidly reossified in the rabbit, the same process may take months or years in man and may never be consummated. This leads to a patchy increase in density and allows time for areas of collapse to occur at the junction of dead and reossified bone. These areas of collapse, and the degenerative arthritis that they may produce, further contribute to increase in density of the involved bone.

Six roentgenograms; 6 photomicrographs; 1 graph.

JOHN P. FOTOPOULOS, M.D.
Northwestern University Medical School

Longitudinal Stress Fractures. Another Variety Seen in Long Bones. M. B. Devas. *J. Bone & Joint Surg.* 42-B: 508-514, August 1960. (12 Richmond Rd., Bexhill-on-Sea, Sussex, England)

Stress fractures in long bones are commonly transverse or oblique, the latter often extending through only a part of the cortex of the shaft. In any instance, only a short length of the bone is involved. The clinical and

radiological findings in 6 examples of longitudinal stress fractures of the tibia and femur are presented.

Longitudinal stress fractures have been seen in athletes, in the middle aged, and in the elderly. The patient usually complains of pain and tenderness in the shin (or thigh) coming on gradually over a period of several weeks or months; the pain is worse with activity, but there is a varying degree of aching at rest. Swelling, which is worse toward the end of the day, may be quite severe, particularly when the lower part of the tibia is involved in older patients. Associated with the swelling in this older group are increased heat and redness. Sometimes a hard lump may be felt attached to the tibia. Forced distraction or bending of the bone may cause pain in patients with an extensive fracture, but may produce no more than slight discomfort in those with smaller fractures.

Radiographs may not disclose any abnormality for some weeks. Occasionally a periosteal haze is observed over one surface of the bone earlier than the fracture itself. In other cases, particularly those of abrupt onset, the fracture may be seen immediately, but this is unusual. The length of the periosteal reaction may indicate the longitudinal nature of the fracture, which is difficult to visualize radiographically, especially if the fracture extends up one cortex only. Oblique views may be necessary before the fracture line can be demonstrated.

Differential diagnosis is important. In the athlete a sarcoma or other tumor may be suspected. Subacute osteomyelitis may be suggested by the swelling, increased heat, tenderness, and the radiographic picture. Infective periostitis, thrombophlebitis, varicose periostitis, and intermittent claudication may all be considered as possibilities if the true nature of the lesion is not recognized. In only 3 of the author's 6 cases was the initial diagnosis correct.

According to the severity of the symptoms, treatment will vary from simple abstinence from sports and excessive activity to immobilization in a full length plaster cast. In all patients in the present series, the fracture united.

Nineteen roentgenograms: 1 photomicrograph: 1 table.

JOHN P. FOTOPOULOS, M.D.

Northwestern University Medical School

Parosteal Osteogenic Sarcoma. Trygve Aakhus, Oddvar Eide, and Torvald Stokke. *Acta radiol.* 54: 29-40, July 1960. (The Norwegian Radium Hospital, Oslo, Norway)

Parosteal osteogenic sarcoma is a rare type of osteogenic sarcoma, probably arising in periosteal connective tissue. It is not yet established whether this tumor is primarily benign with a tendency to growth and to malignant change or whether it is malignant from its outset. Most writers stress the slow growth, the likelihood of recurrence after local excision, and the protracted course of the tumor.

The authors report 5 cases selected from 85 of osteogenic sarcoma in 245 patients with primary malignant bone tumor treated at the Norwegian Radium Hospital from 1932 to 1957. Thirty-four examples of this tumor have been previously recorded in the literature.

A survey of the 39 cases of parosteal sarcoma now on record showed no sex predilection. As compared to ordinary osteogenic sarcoma, the tumor is found predominantly in older patients: this may be explained

in part by its slow growth. The duration of symptoms may extend over a period of months or years, twenty-four years in one case. An indolent, occasionally tender, firm, and fixed swelling has been detected clinically. In most cases the tumor arose in the supracondylar region of the femur as a relatively painless swelling interfering with the movements of the knee.

The parosteal osteogenic sarcoma appears on the roentgenogram as a juxtacortical, broad-based, densely ossified mass, usually at the lower metaphysis of the femur. The base of the tumor is the most sclerotic. The less dense periphery is lobulated or irregular, but usually clearly defined. Within the tumor, scattered rarefactions, corresponding to cartilaginous and fibrous areas or irregular cancellous bone, may be seen. The mass is attached to the cortex along a part of its base and tends to encircle the shaft; a clear zone of varying length may thus be observed between the tumor and the bone. Periosteal lipping and spicules, typical of the ordinary osteogenic sarcoma, are characteristically absent. The appearance of the tumor may remain unchanged for years. As progression ensues, cortical destruction and medullary invasion become evident, and separate ossified masses may appear in the adjacent soft tissues. These changes are particularly noticeable after an attempt at local excision.

The histologic picture varies not only from lesion to lesion but also from one region to another within the same tumor. The fact that the sarcomatous nature of this lesion may be apparent only in scattered small foci makes the histologic diagnosis uncertain, and the choice of treatment difficult.

In the differential diagnosis, myositis ossificans, ossifying subperiosteal hematoma, osteochondroma, and sclerotic osteogenic sarcoma must be considered. The original diagnosis in the authors' 5 cases was osteogenic sarcoma of low-grade malignancy, osteoma, osteochondroma, and fibrochondro-osteoma.

Of the 39 patients, 8 died after an average of eight years (range, four to eighteen years); 1 of these was treated primarily by irradiation and 7 by local excision. Twenty-one were reported alive after an average of seven years, 5 after primary amputation and 16 after primary excision. In 10 patients death was due to other causes or reliable information was not available.

A fairly common history in parosteal osteogenic sarcoma is that of an "atypical osteochondroma," treated by excision and repeated surgery for recurrence, perhaps leading ultimately to extensive metastases. The metastases may also exhibit a slow rate of growth. There is little evidence that radiotherapy is of any benefit. Permanent cure by local excision of the tumor can be expected only in those cases permitting radical extirpation with a fair margin of normal bone and soft tissue. Recurrence after local excision is extremely common and often in a more malignant form. Amputation should therefore be performed if the tumor recurs.

Ten roentgenograms: 1 photograph: 9 photomicrographs.

JAMES F. MARTIN, M.D.

Bowman Gray School of Medicine

Chondroblastoma: A Rare Primary Bone Tumor. H. R. Renfer. *Radiol. clin.* 29: 288-297, September 1960. (In German) (Bern, Switzerland)

Chondroblastoma is a rare nonmalignant epiphyseal bone tumor, occurring predominantly in males during the second decade of life. Less than 60 cases have thus far been reported.

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The neoplasm is frequently confused with giant-cell tumor, chondromyxofibroma, and myxosarcoma. Histologically, it resembles myxochondrosarcoma to such an extent as to be considered its benign variant by some investigators. Because of the difficult histologic differential diagnosis, characteristic roentgen features are most helpful in ruling out a malignant neoplasm.

A case is reported in a male, aged sixteen, who gave a history of a sprain of the left knee about a year earlier, with slight exudate and limited motion. Recent roentgenograms showed a round defect of the internal tibial tuberosity bulging into the joint space and containing irregular small calcific densities. A lesion of the cruciate ligaments could be excluded with the aid of tomograms and arthrography. The tumor was excised and found to be a benign chondroblastoma. Complete relief of symptoms followed an uneventful recovery.

Chondroblastoma occurs mostly in adolescents, with an 80 per cent preponderance of males. It is confined to the epiphyseal portion of long bones. Sites of predilection in the order of frequency are the femur, greater tuberosity of the humerus (Codman's tumor), tibia, and iliac bone. Rare locations are the os calcis, talus, phalanges, and vertebrae. In the smaller bones the lesion can rarely be distinguished from enchondroma. Simple curettage is usually sufficient to effect a cure. Occasionally, postoperative roentgen therapy may be advisable for the prevention of recurrences.

Three roentgenograms: 3 tables; 1 photograph.

ERNEST KRAFT, M.D.
Northport, N. Y.

Prolonged Evolution of Osseous Sarcoma Belonging to the Reticular Group (Reticulum-Cell Sarcoma and Ewing's Sarcoma). Study of Three Cases. L. Lauwers. *J. belge de radiol.* 43: 339-350, 1960. (In French) (Institut Bordet, Brussels, Belgium)

Three cases of slowly developing tumors of bone are presented, the diagnosis being reticulum-cell sarcoma. Two of these were said to be of the Ewing type, so that apparently these two terms are not applied to separate entities in France.

In 2 of the patients the evolution was particularly slow, being twenty-two and twenty-seven years respectively. Intercurrent metastases were efficiently treated by radiotherapy. In the third case the diagnosis was established only after six years.

Four roentgenograms; 1 photograph; 1 table.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Metaphyseal Fibrous Cortical Defect and Non-Ossifying Fibroma. J. Fiset. *J. belge de radiol.* 43: 317-338, 1960. (In French). (Université de Liège, Belgium)

Metaphyseal fibrous cortical defect and non-ossifying fibroma are but different expressions of the same entity. The metaphyseal cortical defect represents the usual regressive form; when the lesion develops progressively and becomes more voluminous, we have the non-ossifying fibroma.

The metaphyseal fibrous cortical defect is usually apparent as a radiolucent area, 1 or 2 cm. in diameter, rather well demarcated, on one side of the distal end of the shaft of a long bone. Relatively little sclerosis is noted about the margin. The non-ossifying fibroma may attain a diameter of 5 to 8 cm. and has a more sclerotic border. With experience, one may make a

rather exact roentgen diagnosis, thus dispensing with the need of surgery.

Seven cases are reported.

Fifteen roentgenograms; 4 photomicrographs; 2 tables.

CHARLES M. NICE, JR., M.D., Ph.D.
Tulane University

Circumscribed Skeletal Rarefactions in Osteogenesis Imperfecta. Theodore E. Keats and Constantine S. Anast. *Am. J. Roentgenol.* 84: 492-498, September 1960. (University of Missouri School of Medicine, Columbia, Mo.)

Caniggia and his associates (*Acta med. scandinav.* Vol. 162 (Suppl. 340) 1958) classified all forms of osteogenesis imperfecta into two main groups: (1) the congenital, fetal forms (*fragilitas ossium hereditaria*, *typus Vrolik*) and (2) the late or adult forms (*Ekman-Lobstein disease*). Circumscribed skeletal rarefaction in patients with osteogenesis imperfecta is a rare manifestation of the disease. Five cases which exhibited this entity have been recorded in the literature: all the adult form of osteogenesis imperfecta. The authors have recently encountered in the latter group 2 cases showing circumscribed areas of skeletal rarefaction; 3 other examples of this finding had previously been reported in the literature (Baumann-Schenker: *Radiol. clin.* 19: 332, 1950. *Abst. in Radiology* 57: 360, 1951), and the present authors add 3 cases among 4 members of one family (representing three generations) with osteogenesis imperfecta. In the youngest patient, who had been followed from birth to the age of two and a half, no areas of rarefaction were evident as yet. They were present, however, in his eleven-year-old sister.

The roentgen appearance of the rarefaction in the authors' patients is not that which has been described by Fairbank (*An Atlas of General Affections of the Skeleton*, 1951) as *osteogenesis imperfecta cystica*. In the present cases the lesions bear a certain resemblance in their early development to fibrous dysplasia. Initially they are thin-walled but eventually sclerotic margins develop and irregular thick trabeculae appear. They do not disappear completely. The occurrence of the rarefaction in the skeleton of one child of the family, with the congenital form of the disease, is further evidence for a unitary concept of all forms of osteogenesis imperfecta.

Nineteen roentgenograms.

ROBERT L. EGAN, M.D.
University of Texas, Houston

Milkman's Syndrome—Five Cases of Severe Osteomalacia Following Gastric Surgery. R. L. Du Berger, G. Masson, and J. Sylvestre. *J. Canad. A. Radiologists* 11: 57-66, September 1960. (Hôpital Général St-Vincent de Paul, Sherbrooke, Que., Canada)

Severe osteomalacia was demonstrated in 5 patients two to sixteen years after gastric resection for peptic ulcer. Each manifested malnutrition secondary to the "dumping syndrome." The ages at operation were twenty-three to thirty-four years; symptoms due to osteomalacia appeared one to four years later. Some or all of the roentgen features of adult osteomalacia—fracture, pseudofracture, and demineralization of bone, with cortical thinning and trabecular rarefaction—were present in each case.

In 2 patients examination with a barium-glucose suspension showed jejunal dilatation, mucosal edema, dilation, and segmentation of barium in the small

intestine. These findings coincided with a 25 per cent decrease in plasma volume. On re-examination of 1 patient with a barium-water suspension, these abnormalities were much less marked. The authors point out, however, that roentgen demonstration of the "dumping syndrome" cannot predict the extent or severity of associated malabsorption, an asymptomatic form of the syndrome having recently been established.

On the basis of animal studies in which the severity of post-gastrectomy osteomalacia was inversely proportional to age, and their own personal experience, the authors conclude that the younger patient has a greater likelihood of developing postgastrectomy malabsorption and resultant osteomalacia.

Twenty-five roentgenograms, 3 graphs; 1 table.

PHILIP M. JOHNSON, M.D.
Montclair, N. J.

Myositis Ossificans Progressiva. M. G. Varadara-jan and Arthur Daniel. *Current M. Practice* 4: 520-528, October 1960. (Government General Hospital, Madras, India)

Myositis ossificans progressiva is characterized by progressive ossification of the muscle sheaths, tendons, and intervening connective tissue beginning before birth or in early childhood, usually before the sixth year. About 200 cases have been recorded in the literature. Three are added in this paper, for 1 of which a relatively detailed report is given.

During the earliest phase of the disease and before the formation of extraskeletal bone, roentgen examination shows only soft-tissue swellings of water density. As early as the first year of life it may be possible to demonstrate narrow band-like bone shadows running longitudinally in the muscles of the back. Irregular bands of ossification are found in various portions of the body: the cervical region, particularly the sternocleidomastoid area; the ribs and scapular area, especially the connective tissue about the axillary muscles; the ligaments of the spine. Ossification is seen also about the pelvis, particularly in the region of the hips and about the muscles of the thighs. In the radiographs of adolescents and adults, irregular spikes or bands of bone are seen in the soft tissues, particularly noticeable in the region of the ribs and scapulae, the lumbar areas, and pelvis. Spurs of bone may project into the pelvis from the bony walls and, similarly, spurs may be seen jutting out from the long bones of the extremities, which usually show thinning of the compact cortex and absence of internal cancellous trabeculation. The little finger may be shortened and deflected by a shortening of the middle phalanx and obliquity of the articular surface of its head. Exostoses may be seen projecting from the upper third of the fibula.

According to recent studies, roentgen therapy may impede the formation of bone in the muscles.

Differentiation must be made from myositis ossificans circumscripta, multiple exostoses, myositis fibrosa, dermatomyositis, parasitic muscular calcification, miscellaneous muscular calcifications, and interstitial calcinosis.

Eleven roentgenograms; 2 photographs; 1 diagram.

Non-Tuberculous Pyogenic Osteomyelitis of the Spine. A. J. Richards. *J. Canad. A. Radiologists* 11: 45-49, September 1960. (Regina General Hospital, Regina, Sask., Canada)

In ten years 11 cases of pyogenic vertebral osteomyeli-

tis were found in 10 patients, including 2 children. The diagnosis was established pathologically in some cases; clinically in the rest. The lumbar spine was involved in 6 instances, the dorsal spine in 3, and the cervical and sacral areas in 1 case each. Narrowing of the intervertebral space occurred in 10 cases, 9 of which exhibited involvement of both adjacent vertebrae. There was a paraspinal mass in 7 cases and neural arch involvement or erosion of the free vertebral margin in 3 cases each. Bone destruction varied from none to very severe, but generalized rarefaction of the involved vertebra was never present. All patients observed over a sufficiently long period showed eventual sclerosis, which occasionally progressed to vertebral fusion. Antecedent infections from which pyogenic organisms may have metastasized to the spine were present in only 4 instances and involved the lower urinary tract in 2.

The author concludes that the most reliable early sign of osteomyelitis is thinning of the intervertebral space with indistinctness of the adjacent vertebral cortical plate. Although absolute radiological differentiation between tuberculous and non-tuberculous vertebral osteomyelitis is not possible, in the latter the course is more rapid, the destruction and collapse are less severe, rarefaction is less marked, and sclerosis is conspicuous during the healing phase.

Four roentgenograms; 4 tables.

PHILIP M. JOHNSON, M.D.
Montclair, N. J.

Avascular Necrosis of the Femoral and Humeral Heads after High-Dosage Corticosteroid Therapy. Walter G. Heimann and Robert H. Freiburger. *New England J. Med.* 263: 672-675, Oct. 6, 1960. (New York Hospital-Cornell Medical Center, New York, N. Y.)

Four cases are reported of avascular necrosis of the femoral and humeral heads following systemic treatment with unusually large doses of corticosteroids for diseases that are not known to produce avascular necrosis of bone (erythema multiforme bullosum, pemphigus, multiple sclerosis, and thrombotic thrombocytopenic purpura).

The mechanism of the production of this complication of corticosteroid therapy in high dosage has not been definitely established. Increased viscosity and hypercoagulability of the blood, as well as cortisone-induced or cortisone-activated vasculitis, are possible causes. Avascular necrosis of the femoral head of unknown etiology occasionally occurs. The possibility that all of the present cases represent an idiopathic avascular necrosis seems unlikely, however, and since the common feature in all was the administration of unusually large doses of corticosteroids, the authors believe that they may be dealing with a newly recognized complication of such therapy.

Four roentgenograms. W. J. VARLEY, M.D.
Mercy Hospital, Pittsburgh, Penna.

A Radiographic Study of the Cuboid in Newborn Indian Infants. K. N. Bhargava and T. C. Garg. *J. Indian M. A.* 35: 200-206, Sept. 1, 1960. (Gandhi Medical College, Bhopal, India)

Three hundred infants (160 males, 140 females) were examined radiologically within two hours of birth in an investigation of the effects of various factors, such as body weight, crown-heel length, sex, race, and parity of the mother, on the various ossification centers of the foot, particularly the cuboid. In 160 of the infants (83

males, 77 females), the center of ossification for the cuboid was found to be present. In 20 infants there were two centers of ossification for the cuboid bone and in 3 infants more than two centers: in 1 infant as many as four centers could be visualized. As would be expected, the frequency of appearance of the cuboid center increased with higher birth weight, longer gestational age, and longer heel-crown length. No definite relationship could be established between the parity of the mother and skeletal maturity. In the lower birth-weight groups, there was not much difference in skeletal maturity between the male and female infants, but in the higher birth-weight groups females showed slightly more advanced ossification than males. Ossification of the cuboid was bilaterally symmetrical.

A comparison of the authors' data with those of Christie (Am. J. Dis. Child. 77: 355, 1949. Abst. in Radiology 54: 301, 1950) disclosed that Indian infants are skeletally more mature than white infants at birth and at par with Negro infants. In all cases where the cuboid center can be visualized radiographically *in utero*, it may be assumed that the fetus has attained a high degree of physiological maturity. Its specific appearance during the ninth month of intrauterine life may help in establishing the age of the fetus.

Four roentgenograms: 3 tables.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

GYNECOLOGY AND OBSTETRICS

Advanced Extrauterine Pregnancy. H. G. Dixon and D. B. Stewart. Brit. M. J. 2: 1103-1111, Oct. 15, 1960. (University College of the West Indies, Jamaica, W.I.)

Extrauterine pregnancy is fraught with danger for both mother and child. Maternal mortality as high as 30 per cent has been recorded, and a fetal mortality ranging from 60 to 90 per cent. The authors report 10 cases of extrauterine pregnancy, with survival of all the mothers and 4 infants. The 10 cases are reported along with one in which the condition was incorrectly diagnosed. The paper is concerned largely with the physical findings and the management, but a short section is devoted to radiology.

Various "pathognomonic" x-ray findings have been described as characteristic of extrauterine pregnancy. Transverse lie is common, and was found in 6 of the 8 cases of this series examined radiographically. Snow (Roentgenology in Obstetrics and Gynecology, 1952) has suggested that the fetus lying transversely inside the uterus usually lies back downward with its extremities directed cephalad, but that the extrauterine fetus commonly lies back uppermost, with extremities directed down toward the maternal pelvis. This theory was supported by 4 cases, but in 2 the fetus was back downward. The attitude of the fetus can best be described as exceedingly odd, though there is no characteristic position, as each fetus has to adapt itself as best it can to the space available for it. In some the spine is hyperextended, in others flexed, but almost invariably the head and/or the limbs are at unusual angles to the trunk. A limb stretched down into the maternal pelvis is especially significant. The appearance of fetal parts overlapping the maternal spine in the lateral view seems to be quite a reliable indication of extrauterine pregnancy (and the only one the authors consider conclusive); its absence, however, does not ex-

clude extrauterine pregnancy. The extrauterine fetus may remain in a singularly constant position and attitude in repeated radiographs. Hysterography is held to be contraindicated except to confirm the diagnosis.

Three roentgenograms; 5 photomicrographs; 2 tables.

JOHN P. FOTOPoulos, M.D.
Northwestern University Medical School

Arteriographic Investigation in Obstetric Pathology. G. Pescetto, P. Valli, and G. Reggiani. Minerva ginecol. 11: 779-787, Oct. 15, 1959. Abridged English translation in Panminerva med. 2: 495-500, October 1960. (Università di Genova, Italy)

The authors carried out arteriographic studies in the field of obstetrics with particular reference to pathological conditions. This type of investigation, they believe, though it will never become routine may have some value for research. Roentgenograms of 5 cases are reproduced: normal pregnancies at the fifth month and at the eighth month; extra-uterine pregnancy in the third month; 2 cases of vesicular mole.

During pregnancy the uterine artery appears enlarged and loses most of its tortuosity. With the gradual rising of the fundus, a modification of the course is observed in the bottom branch according to the stage of the pregnancy, the vessel becoming progressively straighter until it looks like a direct continuation of the uterine artery; the intramural branches, which are not often visible in arteriograms of nonpregnant women, can be seen from the third month onward (especially those branches which supply the placental area). In this site the branches are especially numerous and at their ends present a markedly tortuous appearance. These are the so-called "glomerular arteries," which communicate directly with the placental sinuses without any connection with the capillaries. The placental sinuses are in the great majority of cases clearly visible and unmistakable: on the arteriogram obtained a few seconds after the introduction of the contrast medium, they are characterized by areas of nonhomogeneous capacity; they lie together and have indistinct outlines. The contrast medium brings about a total opacity, which enables the implantation site of the placenta and its size to be determined.

The venous drainage of the placenta is not always clearly visualized.

The authors believe that the amount of radiation given to the pregnant woman in these studies was no more than that from an examination of the digestive system or pelvimetry. They assert that it does not appear from the literature that harmful effects on the fetus follow such examinations.

Fifteen roentgenograms.

THE GENITOURINARY SYSTEM

Experience with Antidiuretic Hormone in Excretory Urography. A. Richard Kendall. J. Urol. 84: 577-581, October 1960. (University Hospital, Ann Arbor, Mich.)

The ability to obtain satisfactory excretory urograms depends in the majority of cases on three main factors: (1) the prevailing renal function, (2) the concentration of the radiopaque medium in the renal collecting system, and (3) extrarenal factors, such as the intestinal gas pattern. Unfortunately, the patient's renal function, once stabilized, is essentially fixed, but the second and third factors are certainly variable and subject to

change. With this in mind, the author has investigated the use of antidiuretic hormone (ADH) in the preparation of the "routine" patient for excretory urography.

Seventy-four patients were prepared by the intramuscular injection of 6 to 10 units of aqueous pitressin approximately thirty to forty minutes before urography. Twenty-one of these had voluntary overnight dehydration. The remaining 53 were subjected to no fluid restriction whatsoever, and 16 were primed with at least 500 c.c. of water within one hour of urography. Ninety-five patients were routinely prepared, *i.e.*, restriction of fluids for approximately fifteen to twenty hours prior to urography.

The specific gravity of the urine was determined just before the intravenous administration of the contrast material. Arbitrarily all urograms were placed in one of four groups, depending on the visualization of the collecting system at five minutes. Sixty-two per cent of the urograms obtained with the use of ADH showed good visualization, with 14 per cent considered excellent. In the routinely prepared group, 53 per cent of the urograms were considered to show good visualization, with only 7 per cent classified as excellent.

Of the 95 patients undergoing routine preparation, 25 per cent were believed to have excessive gas or fecal shadows. Of the ADH prepared patients, only 10 per cent were considered comparable. Thirty-seven per cent of the routinely prepared patients and 55 per cent of the ADH prepared patients were thought to have good gastrointestinal preparation. Eight patients were prepared first routinely and then by pitressin administration alone. A significant finding was a definite diminution in overlying intestinal gas following ADH. Otherwise the urograms were considered comparable.

Eighty-eight per cent of the patients in the ADH group had a urinary specific gravity greater than 1.018; the urograms were good or superior in 74 per cent of these. Sixty-six per cent of those not prepared with ADH had a urinary specific gravity greater than 1.018; the urograms of 60 per cent of these patients were considered good or superior. Thirty-nine patients had a urinary specific gravity of less than 1.018; in only 44 per cent were the urograms satisfactory. It is therefore concluded that a urinary specific gravity in excess of 1.018 is desirable prior to urography.

Only 9 of the 74 patients given ADH exhibited any side effects: mild, fleeting abdominal cramping pains, 1 patient; nausea, 1; precipitous bowel movement, 1; frank emesis 1; mild weakness, not clinically significant, 5.

In general, it can be stated that the use of ADH in the preparation of patients for excretory urography appears to be at least as satisfactory as previous methods and it is certainly more consistent in producing acceptable urograms. The procedure can be recommended for routine usage and is strongly encouraged for older persons in whom actual dehydration is inadvisable. In edematous patients, better urograms are obtained following dehydration and ADH.

The use of pitressin is contraindicated in patients with coronary artery disease and in pregnancy.

One graph; 2 tables. ROBERT BEAROR, M.D.
University of Pennsylvania

A Renal Cortical Index Obtained from Urography Films. A Preliminary Report. P. Vuorinen, L. Pyy-

könen, and P. Anttila. *Brit. J. Radiol.* 33: 622-630, October 1960. (Central University Hospital, Turku, Finland)

The authors present a simple method for measuring and calculating a ratio between the area of the pelvis and calyces and that of the renal cortex. This ratio is termed the renal cortical index (RCI) and is intended to furnish an objective measurement of the functioning renal parenchyma. The RCI is calculated as follows:

$$\frac{C \text{ (mm.)} \times D \text{ (mm.)}}{A \text{ (mm.)} \times B \text{ (mm.)}} = RCI$$

where

- A = Length of the whole kidney in a frontal urography film
- B = Breadth of the whole kidney in a frontal urography film
- C = Length of the pelvicalyceal system in a frontal urography film.
- D = Breadth of the pelvicalyceal system in a frontal urography film.

On the basis of the authors' preliminary studies, the limit value for normal and pathologic RCI lies somewhere around 0.40.

The RCI was correlated with serum creatinine, ureteric calculi, renal tract disease, and age. The mean RCI in 26 patients with normal serum creatinine values was 0.38 as opposed to 0.45 in 20 patients with elevated serum creatinine. In 9 patients who had or had recently had a unilateral ureteric calculus, the mean RCI of the 9 affected kidneys was 0.43 and for the 9 normal kidneys 0.35; the rather low value for the uninvolved kidneys is probably due to compensatory hypertrophy. A group of 31 patients with proteinuria, bacteriuria, cells in the urine, general signs of infection, and elevated blood pressure had a mean RCI of 0.43 as compared to 0.36 in a control group of 23 normal patients. In all, the RCI for 58 normal kidneys and 60 abnormal kidneys was calculated; the mean RCI in the normal group was 0.37 and in the abnormal group 0.44. This difference is considered to be highly significant statistically.

The effect of age on the RCI was evaluated in 17 persons born between 1880 and 1900 and in 20 persons born between 1930 and 1940. An RCI value of 0.41 was obtained for the older group and 0.37 for the younger. These figures correspond to the physiological effects of aging and support the authors' belief that the RCI is really an indicator of functional capacity of the kidney(s).

The results of the observations here reported indicate that the RCI tends to rise in pathological conditions. It is possible that the RCI can form the basis for evaluation of the functional capacity of each kidney separately, which can be important when removal of one kidney is considered. The RCI may be useful also in determining the prognosis in chronic urinary tract disease and in assessing changes in the functional capacity of the kidneys during the course of a disease. It may even be possible to detect unilateral kidney disease through the RCI when this cannot be done by other means.

One roentgenogram; 1 drawing; 3 diagrams; 3 tables. SAMUEL B. HAYESON, M.D.
Lynwood, Calif.

Unusual Urologic Problems in Infants and Children. Edward B. Singleton. *Texas State J. Med.* **56**: 711-719, September 1960. (6621 Fannin St., Houston 25, Texas)

During the five years preceding this report, approximately 6,000 radiographic examinations, including 3,100 intravenous pyelographic studies, were performed in infants and children at the Texas Children's Hospital in Houston. On no occasion was there failure of the injection, due, it is believed, to the routine use of an ordinary scalp vein infusion set for the intravenous puncture (*Am. J. Roentgenol.* **75**: 896, 1956. *Abst. in Radiology* **68**: 458, 1957).

In this paper, 9 unusual cases of the urologic series are reported in detail and some of the more striking roentgenograms are reproduced. These cases include renal lymphoma; renal-cell carcinoma (hypernephroma); ureteral fibroma; müllerian duct cyst; agenesis of the abdominal wall musculature associated with bilateral vesicoureteral reflux, hydronephrosis, hydronephrosis of each upper urinary tract, and an inverted bladder the fundus of which lay below the level of its neck; extensive abnormality of the bladder and upper urinary tracts as the result of congenital urethral stricture; bladder-neck obstruction associated with what were apparently agenesis of one of the kidneys and a solitary renal cyst; a retrocaval ureter; a stag-horn calculus.

Twelve roentgenograms.

Polycystic Renal Disease with Renal and Splenic Artery Aneurysms. Benedict R. Harrow and Jack A. Sloane. *J. Urol.* **84**: 447-452, September 1960. (2621 Biscayne Blvd., Miami, Fla.)

Polycystic disease of the kidneys is a congenital and hereditary condition associated with many different anomalies. In the congenital neonatal form, defects of the central nervous system, genitourinary tract, gastrointestinal tract, and extremities are frequently seen. In the hereditary adult form, usually first manifested by gradual enlargement of the renal cysts in the third, fourth, or fifth decade of life, cysts of the liver and pancreas are the most common accompanying defects.

It is usually not realized that polycystic renal disease is often associated with congenital cerebral artery aneurysm, the so-called "berry" aneurysm. In one series of cerebral artery aneurysms, polycystic disease was found in approximately 6 per cent of the patients; conversely, "berry" type lesions were diagnosed in 16.6 per cent of a group with polycystic kidneys. No account of the association of renal artery aneurysm with polycystic disease was found.

The authors report a case of polycystic renal disease in a patient with a left renal artery aneurysm, right renal calculi, hypertension, and a splenic artery aneurysm. Excretory urography showed bilateral polycystic renal disease and a round calcific shadow adjacent to the medial border of the left kidney. Aortography established that the calcific shadow was the wall of a left renal artery aneurysm. It also revealed the presence of a calcific aneurysm of the splenic artery.

Since, in the authors' opinion, renal artery aneurysms with radiographically calcified rings are not prone to rupture, it was decided not to operate. Some seven months later, however, because of persistent and severe abdominal pain, another surgeon unroofed the left

renal cysts. At that time no aneurysm could be palpated in the hilus of the kidney. It is believed that in this case the renal and splenic artery aneurysms were probably coincidental.

Problems in the management of this patient, as well as the use of translumbar aortography for calcific renal aneurysms, are discussed. The authors believe that aortography should be employed in patients with calcified rings if surgery is contemplated.

Six roentgenograms.

FREDERICK J. MUNSON, M.D.
University of Pennsylvania

Renal Tubular Ectasia in Cystic Disease of the Kidneys and Liver. Bernard J. Reilly and Edward B. D. Neuhauser. *Am. J. Roentgenol.* **84**: 546-554, September 1960. (E. B. D. C., The Children's Hospital, Boston, Mass.)

Renal tubular ectasia or "spongy kidney" is that form of congenital polycystic disease characterized by marked irregular dilatation of the renal collecting tubules but without obstruction and without blind cyst formation. The roentgen appearance should in most instances be diagnostic. The kidneys are increased in size and the irregularly dilated tubules stand out on the excretory urogram like the bare, branching twigs of a leafless bush.

The authors call attention to several aspects of renal tubular ectasia which have not been emphasized by other writers. One is the close association with cystic disease of the liver, so that portal cirrhosis and portal hypertension may cause the presenting signs and symptoms. The other is the hereditary nature of the disorder. Eleven cases are reported to illustrate these points. In 7 of the 11 cases, liver disease was quite definitely present. Five of the patients were members of one family and 2 of another. It is possible that many gradations of polycystic kidney disease, with or without increased connective tissue, may show both hereditary predilection and accompanying cystic disease of the liver.

Apart from its menacing features from association with liver disease, renal tubular ectasia may cause signs and symptoms of renal origin. These are: (1) systemic arterial hypertension; (2) recurrent pyelonephritis; and (3) renal microlithiasis.

Eleven roentgenograms; 2 photographs; 5 photomicrographs.

ROBERT L. EGAN, M.D.
University of Texas, Houston

Milk-of-Calcium Renal Stone: Case Report. W. H. Walker, R. E. Pearson, and N. R. Johnson. *J. Urol.* **84**: 517-520, October 1960. (VA Medical Teaching Group Hospital, Memphis 15, Tenn.)

The milk-of-calcium renal stone is rare. Only one case was found recorded in the English literature for the past thirty-two years (*Howell: J. Urol.* **82**: 197, 1959. *Abst. in Radiology* **74**: 1001, 1960). The authors report the case of a 71-year-old man with adenocarcinoma of the prostate in whom a milk-of-calcium stone of the right kidney was an incidental finding. The patient was admitted to the hospital with a firm, fixed, irregular prostate enlarged to three times normal size. A bone survey disclosed mottled osteoporosis and sclerosis consistent with metastatic carcinoma of the prostate in the skull, ribs, thoracic and lumbar vertebrae, pelvis, and in the femur. Oral

cholecystography showed good concentration of the contrast medium within the gallbladder; in the cholecystograms, a peculiar, half-moon-shaped density was seen in the region of the gallbladder but not lying within the gallbladder shadow. It was thought that this might represent contrast medium, possibly in a diverticulum of the duodenum. A gastrointestinal series was normal. On excretory pyelography, a rounded calcific density, 2.7 cm. in its greatest diameter, was seen overlying the right renal pelvis. A review of the cholecystograms showed, in the upright film, an apparent fluid level of this density parallel to the vertebral column. A transurethral resection of the obstructing prostatic tissue was carried out and a biopsy proved positive for adenocarcinoma. The patient died three days postoperatively.

At autopsy the right kidney appeared grossly normal except for a thin-walled cyst on its posterior aspect. The fluid contained in the cyst was pale yellow in color and was clear except for the presence of minute, granular, calcific particles which formed a paste-like precipitate in the most dependent portion. As the kidney was rotated and the position of the cyst changed, the calcific deposit would flow to the lowermost portion.

The authors conclude that if a calcific density is discovered overlying the renal shadow and is not found to be a true renal calculus or to be within another organ system, an upright film or laberal decubitus film of the renal area should readily establish the presence or absence of a milk-of-calcium renal stone.

Four roentgenograms; 1 photograph; 1 photomicrograph.

WALTER EATON, M.D.
University of Pennsylvania

Perivesical Insufflation of Gas for Determination of Bladder Wall Thickness in Tumors of the Bladder. Osborne Bartley and Hans Eckerbom. *Acta radiol.* 54: 241-250, October 1960. (Sahlgrenska Sjukhuset, Gothenburg, Sweden)

For the past two years, in those cases of bladder tumor in which a study of the perivesical fatty layer alone has not permitted an evaluation of the bladder wall thickness, the authors have employed perivesical insufflation of gas. After the bladder has been emptied as completely as possible, a needle is introduced immediately above the symphysis pubis and directed caudally and dorsally. Its tip should lie about 1 cm. behind and below the upper border of the symphysis and its position should be checked roentgenographically or fluoroscopically. After great care has been taken to ensure that the needle tip has not entered a vessel, 700 to 800 c.c. of oxygen are injected. The patient is then placed in various positions so that the gas may diffuse around the bladder. When the examiner has satisfied himself on this point, and carbon dioxide (generally 200 to 300 c.c.) has been injected into the bladder until the patient experiences a desire to void, both conventional roentgenograms and tomograms are taken.

Eighteen patients have been examined by this technique, and only one complication has been encountered. One patient with a large lymphosarcoma, which displaced the anterior bladder wall 4 to 5 cm. backward and extended as far as the symphysis pubis, suddenly lost consciousness during the injection of the oxygen; the cause could not be established. In view of this experience, the authors feel that injection of gas into the prevesical space should not be undertaken in pa-

tients with large tumors situated in the anterior bladder wall.

With this procedure, it is usually possible to judge the thickness of the bladder wall in the anterior, posterior, and superior and lateral walls, but not in the basal parts. In all but 2 of the 18 cases, there was close agreement between the roentgenographically demonstrated thickness of the bladder wall and the operative findings and the pathologic diagnosis. The two exceptions showed perivesical growth that had not been visualized on the roentgen examination. The method contributes useful information concerning the size and extent of bladder neoplasms.

Six roentgenograms; 1 table.

THEODORE E. KEATS, M.D.
University of Missouri

MISCELLANEOUS

Calcifications in the Peritoneum. E. Balestra. *Radiol. med. (Milan)* 46: 466-474, May 1960. (In Italian) (Università di Genova, Italy)

Using as a starting point a case of radiologically demonstrable calcified peritoneal metastases from a papillary cystadenocarcinoma of the ovary, the author discusses peritoneal calcifications. These are rare when compared with calcifications in the pleura. The morphology of the peritoneal calcifications is not characteristic for several causes, which are given as follows:

1. Peritoneal calculi of uncertain etiology. These may be either fixed or free within the peritoneum.
2. Peritoneal calcification of tuberculous origin. Whereas this is the commonest type of peritoneal calcification, it is much rarer than pleural calcification from the same cause. Radiologically, it may present as rounded heterogeneous opacities, single or multiple; disseminated calcified micronodules; or rounded homogeneous opacities corresponding to calcified cold abscesses.

3. Virchow's "sandy peritonitis." This is a rare form of peritoneal inflammation of unknown cause, seen commonly in females, characterized by hyaline-calcareous cellular degeneration. It has not been dealt with in the radiologic literature. There is similarity grossly between this and the calcified metastases from papillary cystadenocarcinoma of the ovary. The clinical picture is that of a chronic diffuse peritonitis with vomiting, abdominal pain, diarrhea or constipation, and deterioration of the general state of the patient.

4. Dystrophic peritoneal calcification. This is an idiopathic calcific degeneration of the mesenchymal elements of the peritoneum. Although grossly it resembles "sandy peritonitis," it is non-inflammatory, localized rather than diffuse, and affects males as well as females.

5. Cystic calcification. Peritoneal echinococcus and dermoid cysts are not properly varieties of peritoneal calcification, but are here mentioned for completeness.

Three illustrations. CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va

Epidermolysis Bullosa. Case Report. M. Hadley and A. F. MacDonald. *Brit. J. Radiol.* 33: 646-649, October 1960. (Edinburgh Royal Infirmary, Edinburgh, Scotland)

Epidermolysis bullosa is an uncommon skin condi-

tion, characterized by subepidermal bulla formation after relatively minor trauma. Three main types of the disease occur, each with a different genetic background. *Simple epidermolysis bullosa*, with transitory pigmentation and simple bulla formation and without mucosal involvement, is transmitted by a dominant gene and constitutes 45 per cent of cases. *Hyperplastic dystrophic epidermolysis bullosa* with 20 per cent mucosal involvement, frequent papule formation, and often associated with keratosis, etc., is transmitted by a single autosomal gene of high penetrance and accounts for 30 per cent of cases. *Hypoplastic dystrophic epidermolysis bullosa* occurs in 25 per cent of cases and is transmitted by a single recessive gene; it affects both skin and mucous membranes and is associated with xerodermic, presenile skin, absence of the nails, hypoplasia of the jaws, and early dental caries; psychiatric disorders are frequent. Early onset is usual in this type.

The authors report a case which falls into the last category. The diagnosis was initially made when the patient was two weeks old. At the age of twenty-four he was seen because of dysphagia, and a barium swallow revealed a stricture of the lower third of the esophagus. Biopsy of the mucosal lining of the post-cricoid region was interpreted as being consistent with the findings in epidermolysis bullosa. Roentgen examination showed hypoplasia of the mandible with increase in the angle and consequent prognathism; only 2 teeth remained, both unerupted. Roentgenograms of the hands showed hypoplastic metacarpals and phalanges, a decrease in the width of the palms, complete absence of the nails, and small spots of soft-tissue calcification in the tips of two fingers.

The basic histopathology is simply that bullae are formed between the epidermis and dermis in response to trauma, which need only be minimal. Following rupture of the bullae, secondary inflammation and subsequent fibrotic changes take place. As in the present case, the symptoms of the disease are usually due to scar tissue replacement of the skin. The areas exposed to trauma—the hands and forearms—are mainly affected by this fibrotic process. Loss of nails and calcification in the finger tips is probably subsequent to devitalization of the skin and deficient nutrition.

The diagnosis is primarily a clinical one, but the radiologist should be aware of the changes associated with the skin lesions and the various facets with which the disease may present.

Five roentgenograms; 1 photograph.

HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

TECHNIC

Reliability of Pinhole Methods in Evaluation of Radiation from Emission Area in Roentgen Tubes.
Pekka Vuorinen. Acta radiol. 54: 41–44, July 1960. (University of Turku, Turku, Finland)

A device embodying the principle of the pinhole camera, consisting of a small hole in an absorbent plate

between the source of radiation and the film, is generally employed for roentgenograms of the focal spot and off-focal radiation. The author describes an investigation of the effect of changes in the shape, size, and position of the pinhole upon the images obtained. By using actual radiographs, he found that markedly different intensity distributions (apparent in the degree of blackening of the film) result when the size, shape, and position of the pinhole are varied. He points out that the films cannot be wholly relied upon in the evaluation of the radiation of the different parts of the emission area. The film gives a true representation of the beam of radiation between it and the pinhole and the same holds true for all pinhole methods, regardless of the recording device.

Nine roentgenograms. ROBERT C. McLANE, M.D.
Bowman Gray School of Medicine

Factors Determining Quality in a Radiograph with a Discussion of Film Faults and Artefacts. D. C. Eaglesham. J. Canad. A. Radiologists 11: 67–74, September; 89–95, December 1960. (Guelph General Hospital, Guelph, Ont., Canada)

The author discusses 9 groups of factors affecting film quality. *Resolution* (sharpness, definition) is necessarily limited by the inability of the unaided human eye to differentiate lines less than 0.1 mm. apart. Factors affecting resolution in greater or less degree are: (a) motion of subject, film or x-ray tube, (b) screen quality, (c) focal spot size, (d) object-film distance, (e) exposure, (f) film "graininess," and (g) parallax. *Contrast*, the difference in opacity between the lightest and darkest areas of the image, is essential to recognition of detail. Non-screen film has the greatest inherent contrast but screens markedly enhance contrast. Increase in the kvp/mas ratio directly or by beam filtration reduces contrast, as does under- or over-exposure, sub-optimal development time, developer fog and stain, and secondary radiation including back-scatter. Glare during illumination of the processed film adversely affects contrast. *Gradation* or scale, the number of densities intermediate between the extremes of the contrast range, is reduced by use of screens and by underdevelopment but is increased by higher kvp.

Film opacity, sensitivity, exposure latitude and physical qualities also help determine radiographic quality. Additional factors are radiographic composition and freedom from artefacts.

Artefacts are due to any of a variety of faults in processing, faults during exposure, and faults inherent in the film. Also to be guarded against are the screens themselves; the so-called overlap density paradox in which the expected summation effect of superimposed shadows is reversed; errors in marking for identification; stereoscopic depth failures; errors in medical technic (barium mixture faults; unsatisfactory patient preparation). By close attention most of these errors will be eliminated and the radiologist's reputation for good work will be as unblemished as his films.

Four roentgenograms. PHILIP M. JOHNSON, M.D.
Montclair, N.J.

RADIOTHERAPY

Radiation Therapy in the Management of Neoplasms of the Central Nervous System, with a Special Note in Regard to Children: Twenty Years' Experience, 1939-1958. Jean Bouchard and Carleton B. Peirce. *Am. J. Roentgenol.* 84: 610-628, October 1960. (Royal Victoria Hospital, Montreal 2, Quebec, Canada)

The authors present their twenty years experience with the irradiation of neoplasms involving the central nervous system, based on a total series of 826 cases, including 534 which were adequately treated five to twenty years ago. Patients were considered to be adequately treated who had received a tumor dose within the range of dose-time relationship which could be expected to be potentially capable of controlling the neoplastic process and possibly have a curative effect. For the most part this meant 5,000 to 6,000 r (at 220-280 kv) in approximately fifty days.

The present discussion centers on 399 patients with primary intracranial tumors who were seen between 1939 and 1953. Eighty-nine of the 399 patients (22.3 per cent) were still living at the time of the report, five to twenty years after irradiation. One hundred and thirty-one (32.8 per cent) survived five years or more after diagnosis and treatment. The majority (88 per cent) were treated postoperatively, chiefly because of presumably incomplete removal of the tumor. The remaining 12 per cent were treated by irradiation alone, without any attempt at surgical removal of the tumor. Of the 399 tumors, 78.5 per cent were classified as gliomata.

Glioblastoma multiforme has the poorest prognosis of all the malignant gliomata. Twenty per cent of 125 patients lived more than two years. Only 4 were still alive seven, nine, eleven, and fourteen years after diagnosis and initiation of treatment. In glioblastoma, the authors believe that the combination of irradiation with surgery offers a definite advantage.

Eighty-one patients with *astrocytoma* were treated, with a ten-year (or better) survival rate of 35.8 per cent. Comparison of these results with those in a surgically treated series shows that patients treated by surgery and irradiation may expect a much greater longevity.

The *unclassified gliomata* (30 cases) responded slightly less well than the astrocytomas, with 6 patients living over ten years.

In *medulloblastoma* (41 cases), the survival rate appeared rather favorable, but it was markedly less than that recorded by others. The three-year survival rate was only 29.2 per cent. Only 5 of the patients had involvement of the spinal axis. Of the 6 of the 41 patients who were subjected only to biopsy before irradiation, 2 were alive more than ten years after treatment.

Only 12 cases of *ependyoma* and *ependymoblastoma* were encountered. The entire cerebrospinal axis was irradiated in only 1 case. The ten-year survival rate was 50 per cent.

Oligodendroglioma and *oligodendroglioblastoma* are even more uncommon types of gliomata. The authors' material comprises only 9 cases, which were irradiated either because of more malignant character than usual or in view of definitely incomplete surgical removal. Although 5 of the patients survived over five years, only one had lived for more than ten years at the time of the report.

Mid-brain and pontine tumors are infrequently ac-

cessible even for biopsy. In only 7 of the 20 tumors located in the mid-brain in the present series was the histopathologic type of neoplasm known. The overall five-year survival rate for patients with mid-brain tumors was 40 per cent with irradiation alone. In only 1 of the 21 pontine tumors was a histopathologic diagnosis possible. Four of the 21 patients irradiated on the basis of a clinical diagnosis only have survived ten years or longer.

Of the 16 patients with *malignant meningiomas*, 57.1 per cent survived ten years or longer after treatment with surgery and adequate irradiation.

Eleven of 13 patients with *intracranial sarcoma* were treated by surgery and irradiation, with a ten-year survival rate of 30.8 per cent.

Fourteen *blood-vessel tumors*, of various histopathologic types, all in adults, were irradiated. Only 4 patients in this group have died, 3 of unrelated causes. Most of the patients have been able to resume useful lives. The hemangioendotheliomas (2 cases) were given the highest tumor dose of all, from 5,000 to 6,000 r in forty-five to fifty days.

Twenty-seven patients with *metastatic tumors* to the brain were treated; 7 of these patients were referred with a diagnosis of primary intracranial tumor, later proved metastatic. Only 7 of the entire group showed no improvement following irradiation. Seventeen returned to normal clinically for varying periods of time—enough to warrant treatment. Lung and breast cancer accounted for 13 of the 27 cases, with the primary source undetermined in 4.

Special consideration is given to 79 children (under fifteen years of age) who are included in the series of 399. Medulloblastomas accounted for 28 (35.5 per cent) of these cases. Only this tumor had a greater incidence in children than in adults. In 22 of the 79 children, there was no surgical removal of the tumor. Twenty-five (31.7 per cent) of the children were still living five to twenty years after irradiation. The five-year survival rate for the entire group was 38.0 per cent. The tumor doses for these young patients were usually less by a factor of approximately 20 per cent than those employed in adults. Only 4 of the 30 children who have survived over five years after irradiation are not perfectly well. Not one has shown signs of postirradiation damage to the pituitary gland. No disturbances of normal growth and development have been observed. A direct comparison of five-, ten-, and fifteen-year survival rates indicates that children, in general, can be expected to do as well as, and probably better than, adults in terms of long and useful survival.

The authors emphasize the importance of the quality of survival after surgery, irradiation, or both, in the treatment of primary or metastatic brain tumors. To achieve adequate irradiation with virtually no post-irradiation complication, it is felt that increased intracranial pressure must be controlled with effectiveness and that irradiation be accomplished in a single protracted course with an optimum dose-time relationship. The authors are particularly encouraged by the favorable results in mid-brain and pontine angle tumors treated by irradiation alone. In no case has opacification of the ocular lens been detected that could be attributed to the radiation therapy.

Eighteen tables. DAVID L. ROBINSON, M.D.
Barksdale AFB, La.

Treatment of Head and Neck Cancer. Janeway Lecture, 1960. William S. MacComb. *Am. J. Roentgenol.* 84: 589-609, October 1960. (M. D. Anderson Hospital and Tumor Institute, Houston, Texas)

The author discusses the progress and treatment of patients with head and neck cancer by surgery and by radiotherapy and by the combined use of both modalities. Following an historical account, he reviews the past eight years experience at the M. D. Anderson Hospital (Texas), covering 416 cases. The choice of treatment depends upon the site and extent of the disease at the time of the patient's admission to the Head and Neck Clinic. In general, patients with lymphomas are treated by irradiation, those with salivary gland tumors and tumors of the thyroid are treated surgically. Sarcomas, aside from lymphosarcoma, are comparatively rare in the head and neck region and, except for lymphosarcomas, are a surgical problem. Squamous-cell cancers at the above institution make up the largest percentage of malignant tumors and frequently both surgery and radiation therapy are needed.

Irradiation is felt to be the treatment of choice for most intra-oral squamous-cell carcinomas. Various combinations of external radiotherapy and/or interstitial low-intensity radium needles are utilized in the management of these tumors. Most are quite radiosensitive and reasonably accessible. Cancers arising in the oropharynx (including the palatine arch) and the pharynx (faucial tonsil, base of the tongue, and pharyngeal wall) usually receive radiotherapy. Local metastatic areas, when present, are included in the treatment field of the primary lesion. If tumor regression is incomplete or reactivity occurs, then a surgical attack is instituted. Early cancer of the intrinsic larynx also seems best managed by external radiotherapy. Early tumors of the supraglottic region may be successfully treated by irradiation, but when invasion of cartilage is well established response is not usually favorable. Tumors of the larynx which have undergone radical radiotherapy may still be treated by total laryngectomy, should the former fail, without fear of increasing the morbidity of the surgical procedure.

Tumors best treated primarily by surgery include many tumors of the skin and lip and occasionally very early lesions of the oral cavity in readily accessible regions. Carcinomas of the hard palate and upper gingiva are entirely surgical problems, as are many tumors of the supraglottic region of the extrinsic larynx. For malignant disease of the cervical esophagus, surgical excision is preferred.

In many instances of head and neck cancer the combined use of radiotherapy and surgical excision may offer the patient the best chance of control. "Planned combined therapy" is particularly useful in patients with cervical lymph node metastases from intra-oral cancer. "Were the surgical procedure alone to be used for the complete extirpation of the (advanced intra-oral) primary lesion, the amount of intra-oral tissue to be removed would be so great that primary closure would be difficult and the functional result for the patient would be unsatisfactory. By using radiation therapy before surgery, at times delivering slightly less than a full tumor dose, the amount of tissues to be excised from the primary site is decidedly less than would have been necessary with surgery alone. Increased morbidity following pre-operative irradiation and surgery is recognized, but this fact is more than offset by the improved prognosis and the better functional result

obtained for the patient. Delay in healing sometimes does occur. If radiation given through the operative region is not over 6,000 r tumor dose little difficulty in healing will be encountered."

Under the heading "unplanned combined therapy" are considered cases ordinarily successfully treated by one modality or the other, but in which recurrence or reactivation of the primary lesion necessitates further therapy. In general, recurrences following initial radiotherapy are managed by surgery, and vice versa.

Much detailed information regarding selection of patients for surgery or radiotherapy with respect to site of origin and tumor extent is presented. Numerous short case histories illustrate the results which can be obtained by combined therapy. Statistical tables show the results achieved in tumors arising in various anatomical sites.

Seven roentgenograms; 11 photographs; 3 tables.

JAMES W. BARBER, M.D.
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Cancer of the Larynx Using Radiation Therapy for Treatment. Galen M. Tice. *J. Kansas M. Soc.* 61: 465-468, September 1960. (Department of Radiology, University of Kansas Medical Center, Kansas City 12, Kans.)

Between Sept. 1, 1930, and Jan. 1, 1960, 140 pathologically verified cases of cancer of the larynx were seen in the Department of Radiology of the University of Kansas Medical Center. Only in more recent years has an adequate description been given on the records, but in a review of these cases, an attempt was made to classify the carcinomas as intrinsic or extrinsic. The five-year survivals in cases treated by irradiation are tabulated as follows:

Type of Case	No.	Five-Year Survival (%)
All cases	140	17
Extrinsic	80	11
Intrinsic	60	25
Early cases, with irradiation only	11	73
Laryngofissure followed by irradiation	11	25
Laryngectomy followed by irradiation	26	35
Total cases treated by definitive surgery followed by irradiation	37	32

The author concludes that cancer of the larynx when far advanced offers an extremely poor prognosis, whether treated by surgery or irradiation. Early cancer of the larynx, Stage I, may be cured in a high percentage of cases by roentgen therapy. Surgery may accomplish the same result, but irradiation leaves the patient with a relatively normal voice.

Three case reports; 2 tables.

Technique for Intracavitary Irradiation of the Nasopharynx. Herman D. Suit, Ralph S. Lloyd, J. Robert Andrews, and Stanley E. Sneider. *Am. J. Roentgenol.* 84: 629-631, October 1960. (J. R. A., National Cancer Institute, Bethesda 14, Md.)

The authors describe a technic for the preparation of an acrylic mold of the nasopharynx, which is used to carry an intravitray source of radiation to supplement external irradiation of certain nasopharyngeal neoplasms. No surgical resection of the palate or nasal septum is required to obtain accurate positioning of the

mold and radiation sources. The precise positioning of the mold permits the fixation of the radiation source either centrally or eccentrically, as required, so as to irradiate mainly the tumor-bearing area. The impression of the tumor residue is demonstrable on the mold and the radiation source can be positioned in relation to the tumor by direct inspection. The patient is under general anesthesia for approximately sixty to seventy-five minutes.

An appropriate mass of black dental impression compound is forced into the nasopharynx by digital pressure. A special cooling tray is used to carry the impression material and by circulating ice water through the tray the compound can be hardened within four minutes. A dental technician then duplicates the mold in Durabase, a pink acrylic. Two ties are attached to the mold at points corresponding to the posterior choanae and to the oropharyngeal surface. The radiation sources are positioned in holes drilled in appropriate sites in the mold. Finally, the mold is placed in the nasopharynx and fixed by the ties.

The authors cite the case of a 5-year-old girl with rhabdomyosarcoma of the nasopharynx. After a tumor exposure dose of 5,000 r had been delivered to the nasopharynx and surrounding tissue by 2 Mev x-rays, a small nasopharyngeal mass persisted. A mold was prepared and by means of radium fixed within it, an additional 3,000 r was given (at 1 mm. tissue depth) in two sessions; only 400 r reached the opposite nasopharynx and the nearest portion of the mid-brain.

Three figures. DAVID L. ROBINSON, M.D.
Barksdale AFB, La.

Roentgen Irradiation as the Exclusive Method or Supplemented by Operation in Laryngeal Carcinoma: Report on 334 Cases. Franz Wachtler. *Strahlentherapie* 109: 343-351, June-July 1959. (In German) (Zentral-Röntgeninstitut der Universität Wien, Austria)

The effectiveness of roentgen therapy (190 kv with a half-value layer of 1.1 mm. Cu) in the treatment of carcinoma of the larynx is assessed on the basis of 334 cases treated during the years 1948 to 1953. Treatment was given over a period of four to five weeks. The skin dose was between 3,600 and 4,000 r, and the calculated tumor dose between 5,000 and 5,500 r. The method employed is discussed in detail.

Of the 216 patients who were treated by radiation alone, 82 (38 per cent) survived longer than five years without signs of recurrence. For the 118 patients who were subjected first to surgery (total or partial laryngectomy) followed by radiation therapy, the five-year survival rate was substantially the same.

Tumors of the glottis (vocal cord carcinomas) had a five-year survival rate without evidence of disease of 46.5 per cent (64 per cent for Stages I and 2). The prognosis was definitely unfavorable in the cases of subglottic carcinoma, lasting cures being rare exceptions. The five-year survival rate of the patients treated for supraglottic tumors was 23.5 per cent. Old age diminished the chances of cure. The prognosis was more favorable with histologically undifferentiated than with differentiated carcinomas.

The principal complications observed in applying radiotherapy to the larynx were perichondritis, early edema, pneumonia, hemorrhage due to erosion of ulcerated tumors, and radiation-induced anorexia with its serious sequelae.

The author concludes that, in spite of expert surgery and radiation therapy, 60 per cent of the total number of cases of cancer of the larynx treated are not cured. Seven tables.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Roentgen Diagnosis and Radiation Therapy of the Thymus Gland. Umberto Cocchi. *Strahlentherapie* 109: 426-440, June-July 1959. (In German) (Röntgendiagnostische Zentralinstitut und Radiotherapeutische Klinik der Universität Zürich, Switzerland)

The normal thymus gland can be visualized in children only if pneumomediastinum is employed. In hyperplasia of the thymus, the organ may be enlarged up to twice or three times its original size, or even more. With the help of schematic drawings the author describes in detail the various types of thymus hyperplasia as seen on the chest roentgenogram.

Since 1921, 111 children with thymus hyperplasia had received radiation therapy at the University of Zürich, with doses to the gland ranging from 37 to 150 rad. Seventy-eight per cent of the children improved within a few weeks, and the reduction of the hyperplasia could be proved by a chest film. Clinical improvement without radiologic change was noted in 6 per cent, radiologic without clinical improvement in 3 per cent, and neither in 13 per cent of the cases.

The author doubts that there is valid proof of the relationship of radiation therapy of a thymus gland and the development of a malignant tumor, particularly in the thyroid. Reported cases in the literature do not sufficiently consider physical factors to justify any conclusions. The University of Zürich has seen 2 cases of carcinoma of the thyroid in children, and in neither of these was there a history of radiation therapy.

Since 1921, about 15 thymic tumors were observed at the University of Zürich. Among these were 2 sarcomas (1 round-cell and 1 highly differentiated lymphosarcoma), 4 thymus carcinomas, 1 benign thymoma, and 8 malignant thymomas. Six of the 15 patients had been subjected to thymectomy prior to irradiation. Ten patients died within several months following treatment; 5 of the 8 with malignant thymoma were alive and symptom-free after twelve months.

Sixteen roentgenograms; 12 diagrams; 3 tables.
EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Eighty-two Cases of Mammary Cancer Treated Exclusively with Roentgen Therapy. A. Hochman and E. Robinson. *Cancer* 13: 670-673, July-August 1960. (Hadassah University Hospital, Jerusalem, Israel)

Eighty-two women from an unselected group of cases of cancer of the breast of all stages were treated exclusively with roentgen therapy. These patients had rejected surgery and were considered to be getting only the second-best treatment. According to Portmann's classification, 4 patients had Stage I cancer; 5, Stage II; 7, Stage II-III; 35, Stage III; and 31, Stage IV.

All 4 patients with Stage I cancer and 3 (60 per cent) of those with Stage II were alive after five years. There were 5 survivors in these two groups after ten years, but only 1 without evidence of local recurrence or of metastatic spread. Of the 7 patients with Stage II-III cancer, 3 were alive after five years, but none lived for ten years. Twenty-one of the 35 patients with Stage III

cancer lived for three years and 7 for five years; none were alive at ten years. None of the patients with Stage IV cancer lived as long as three years. Thus, in the entire series of 82 cases, only 5 patients lived as long as ten years, and only 1 may be said to have been cured, that is, she was still alive after twenty-two years without signs of metastases.

With the passing of the years many of the patients were seen to suffer from late radiation changes, necessitating surgical removal of the breast stump or plastic surgery. In the final analysis it seems that more often than not the irradiated breast was a source of pain and suffering, which makes it doubtful that the effort to preserve the breast was worthwhile.

The authors' conclusions are similar to those of Haagensen and Stout (Ann. Surg. 118: 859, 1032, 1943), that is, patients with Stage I and II breast cancer fare better with surgery, while those with more advanced cancers fare better with radiotherapy.

Four tables.
HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

Results of Radiotherapy of Esophageal Carcinoma from 1953 to 1957. Marianne Gaul and Heinz Karl Parchwitz. *Strahlentherapie* 109: 588-598, August 1959. (In German) (Chirurgische Universitätsklinik Bonn, Germany)

Preliminary to discussion of the results obtained with their newly installed rotational therapy equipment in carcinoma of the esophagus from 1953 to 1957, the authors briefly review their earlier radiation technic. The cases previously treated and reported in 1952 numbered 163. Fourteen patients received a tumor dose of 450 to 3,900 r; a second group received 1,500 to 4,500 r; 2 were treated exclusively with radium; 52 were treated by a combination of roentgen and radium therapy. The latter received 4,000 r plus 120 to 240 mg. hr. radium. The average survival for the entire group was seven and one-half months, a figure in general agreement with that of other workers.

From the institution of rotational therapy in 1953 until the end of 1957, the authors treated 66 patients with carcinoma of the esophagus. Thirty-one patients were subjected to surgery and 35 were treated with irradiation, numbers admittedly too small to permit valid comparative evaluation of the two methods. Pendulum radiation was used at an angle of 330°, a fixed focal distance of 50 cm., and daily fractional doses of 150 to 200 r for a total tumor dose of 5,000 to 6,000 r. The patients were fortified with injections of vitamin B-complex and liver preparations; blood transfusions were also given in some instances.

The malignant growth was situated in the upper third of the esophagus in 22.4 per cent of the patients, in the middle third in 48.5 per cent, and in the lower third in 29.1 per cent. Histologic examination was possible in one-third of the cases and confirmed the roentgenologic diagnosis in every instance. Histologically, there was 1 solid carcinoma, 6 squamous-cell carcinomas, 2 adenocarcinomas, and 2 small-cell carcinomas.

The average length of survival of the 23 patients who received adequate tumor doses was fourteen months, allowance being made for 7 patients still alive. In the 12 remaining patients, either the radiation dose was inadequate to effect tumor regression, the metastatic spread was too advanced, or there was refusal to submit to further treatment.

The palliative effects produced by the radiation therapy were found to be favorable as judged by the following criteria: general tumor regression and disappearance of existing stenoses; ability to swallow solid food; increase in body weight; relief from pain, and physical improvement and mental uplift.

Among the complications were: recurrence of tumor growth along the margin of the tumor bed (5 cases), rapidly eventuating in cachexia; perforation of the esophageal wall with formation of tracheobronchial fistulas (7 cases). In 4 cases, the fistulas did not occur until twelve months after termination of radiation therapy. Further complications rapidly led to a fatal ending, although the autopsy examination showed complete regression of malignant growth.

In a final comment the authors point out that the average survival time was increased from the previous seven and one-half to fourteen months by the rotational technic and tumor dosages from 5,000 to 7,000 r.

Five roentgenograms; 2 photomicrographs; 3 tables.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Primary Neoplasm of the Liver. Results of Radiation Therapy. Ralph Phillips and Koichi Murikami. *Cancer* 13: 714-720, July-August 1960. (Memorial Center for Cancer and Allied Diseases, New York, N. Y.)

The results of radiation therapy in 26 cases of hepatocellular carcinoma are analyzed. In 4 cases the tumor dose was less than 2,000 r and was ineffective. In 22 cases the tumor dose was more than 2,000 r (average 2,956 r in an overall time of twenty-three days). Marked tumor regression occurred in 9 cases in this group and measurable regression in a further 5 cases. Excellent symptomatic improvement was obtained in 11 cases and some improvement in 5. The duration of life after radiation therapy averaged twelve months, which is three times the average total duration generally recorded for this disease.

Patients in this series are not considered typical of those generally seen with hepatocellular carcinoma: the average duration of symptoms and irradiation was longer than is usual (twelve months); the number of male and female patients was equal (instead of males predominating); and 18 of the 26 patients were less than forty-five years of age. The results of treatment, however, were in line with those previously reported for metastatic liver cancer.

The authors propose a method of management of cancer of the liver with a view to complete cure: (1) aspiration biopsy at an earlier stage in patients who have an enlarged liver with typical symptoms of pain, weight loss, malaise, anorexia, and weakness, with biochemical evidence of liver cancer, in whom no primary cancer elsewhere for the origin of liver metastases can be demonstrated; (2) supervoltage x-ray therapy, with a tumor dose of 2,500 to 3,500 r in about three weeks (the useful radiation effects are tumor regression, decreased vascularity of the tumor, reduction in portal hypertension, and improvement of the impaired liver function and electrolyte disturbances); (3) radioactive isotope scan of the liver (using iodinated serum albumin or rose bengal) to determine if one lobe is uninvolved; (4) laparotomy with a view to hepatic lobectomy.

Three tables.
HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

The Effect of Preoperative Roentgen Therapy upon the 10 and 5 Year Results of the Surgical Treatment of Cancer of the Rectum. Stuart H. Q. Quan, Michael R. Deddish, and Maus W. Stearns, Jr. Surg., Gynec. & Obst. 111: 507-508, October 1960. (44 E. 67th St., New York, N. Y.).

The authors analyze the five- and ten-year results in 770 surgically treated patients with primary adenocarcinoma of the rectum seen at the Memorial Center, New York, between 1939 and 1949. Whereas preoperative roentgen therapy did not appear to affect the survival of patients with cancer that had not spread to the mesenteric lymph nodes, it definitely seemed to exert a favorable influence on the survival of patients with tumors with lymph node metastases. Patients in this latter group who had received preoperative irradiation had a 37 and 27 per cent five- and ten-year survival rate. Those who were not given preoperative irradiation had only 23 and 10 per cent five- and ten-year survivals. On the basis of these findings, it is believed that preoperative roentgen therapy is a worthwhile adjunct to the standard radical resections now universally employed for cancer of the rectum.

One table. MARK M. MISHKIN, M.D.
University of Pennsylvania

Radiation Therapy of Primary Carcinomas of the Ovary. Alois Beutel and Willi Ernst Adam. Strahlentherapie 109: 251-256, June-July 1959. (In German) (Röntgeninstitut und der Strahlenklinik der Städt. Krankenanstalten Dortmund, Germany)

The results related in this report on radiation therapy of primary ovarian carcinomas is based on 109 cases seen by the authors between 1949 and 1958. Of the 42 patients treated up to 1953, a cure was obtained in 20.7 per cent, although 50 per cent of these cases were of Stages 3 and 4.

The four successive stages of malignancy recognized by the authors are characterized, respectively, (1) by localization solely in the ovary, (2) by involvement of the surrounding organs, such as peritoneum, omentum and tubes, (3) by extensive metastatic growth throughout the peritoneal cavity, with inoperable or only partly operable tumors, and (4) by metastatic involvement of the vagina, bladder or rectum, and other distally situated organs. Of the 42 primary ovarian carcinomas treated up to 1953, 12 were of the first stage, 8 of the second, 8 of the third, and 14 of the fourth stage. Of the 12 patients with Stage 1 disease, 6 were cured; there were no survivors in the Stage 2 group, but 3 in Stage 3 and 1 in Stage 4. The five-year survival rate for the whole series of 109 patients was 28.6 per cent. The five-year rate for some 2,600 cases reported in the literature varies between 11.6 and 25 per cent.

Operative procedures included: radical resection (83), tumor excision (11), and partial resection (7). Laparotomy was carried out in 7 cases and irradiation alone in 2. The procedure of choice was surgery followed by irradiation; the latter alone was not satisfactory. The presence of the uterus is advantageous for internal radium therapy. Radiation therapy was applied to six abdominal fields, for an average tumor dose of 3,000 r. In cases of upper abdominal involvement, liver and spleen were protected. The average lapse of time between surgery and the beginning of radiation therapy was six weeks.

All except 10 of the 109 patients were over forty years of age. A considerable variety of histologic

types were encountered, but in general it was not possible to make a prognosis based on the histologic findings prior to therapy.

Three tables. EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Choice of Treatment of Carcinoma of the Bladder. Eric Riches. J. Urol. 84: 472-480, September 1960. (22 Weymouth St., London W. 1, England)

The author describes two types of bladder carcinoma clinically, papillary and solid, although the differentiation between the two is not always clear-cut. In general, papillary tumors tend to be diffuse and multiple and to invade the bladder wall late, while the solid tumors are usually single or localized, with early invasion of the wall. The depth of penetration of the tumor is known as its stage; the histologic grades, based on cell differentiation are low, intermediate or average, and high. Before any choice of treatment can be made, the minimum investigations required are excretory urography, cystoscopy, cystoscopic biopsy, bimanual examination under anesthesia, and bacteriological examination of the urine. Regardless of the choice of treatment, careful periodic follow-up examinations are emphasized.

Papillary tumors of low-grade malignancy and moderate size are best treated by endoscopic surgical methods. A higher grade of malignancy is an indication for radiotherapy and, if the tumor does not exceed 5 cm. in diameter, radioactive implants are effective. The author has used radon seeds, though more recently he has substituted gold grains. An attempt is made to deliver a tumor dose of approximately 6,000 r. With this interstitial technic, a five-year survival of 70 per cent has been achieved in low-grade tumors and 42 per cent for those of high malignancy.

Various forms of open operation are employed for papillary tumors. With open diathermy excision, the growth is excised down to the muscle layer. In the author's series, 30 per cent of those thus treated survived five years. In 2 patients, the open operation consisted of excision of the bladder mucosa. One of these had two recurrences and the other suffered a contraction of the bladder requiring colocolostomy. Partial cystectomy is applicable to a single large papillary lesion situated on a mobile portion of the bladder. Total cystectomy gives the best promise of complete freedom of recurrence from the disease, but is attended by the difficulties of deviation of the urinary stream into the ileum or colon. The author's five-year survival for 36 total cystectomies was 42 per cent. He feels that this procedure has the best chance of success in patients with extensive multiple papillary tumors of low-grade malignancy.

Intracavitary irradiation with a central source of cobalt 60 placed in a balloon in the bladder has proved disappointing, as has contact x-ray therapy. External irradiation, in 45 cases, 14 of which were papillary and 11 partly papillary and partly solid, gave good palliation in 13, and poor or no palliation in 12.

Solid tumors, in general, have a higher intrinsic degree of malignancy. They are curable only if seen early before invasion has occurred. They are not amenable to endoscopic methods or interstitial or intracavitary irradiation. Whether a partial or total excision of the bladder is done depends on the site of tumor and extent of mucosal change around it. For those cases of solid tumor requiring only partial cystectomy,

the author's five-year survival is quoted as 36 per cent. For those requiring total cystectomy there was a 9 per cent five-year survival.

External irradiation was given to 52 patients, with either the cobalt-60 theratron or 4-Mev linear accelerator. In this group were both papillary and solid tumors. The aim was to give 7,000 r over sixty days. Twenty-one of this series had relatively good palliation and 32 had little or none. Solid appeared to be less responsive than papillary tumors. Distant metastases followed the usual pattern, occurring in the liver and lungs. Of the side effects of supravoltage therapy, bladder contraction, telangiectasia (sometimes with hemorrhage), and rectovaginal or rectovesical fistula were significantly common.

In closing, the author states his conviction that ultimate treatment of the bladder carcinoma will lie in a combination of radiation and surgery.

Ten figures. EUGENE F. FOLEY, JR., M.D.
University of Pennsylvania

Treatment of Malignant Melanoma. Milan Spoljar, Nikola Franicevic and Milan Kubovic. *Strahlentherapie* 109: 352-356, June-July 1959. (In German) (Radiologische Institut der Universität Zagreb, Hungary)

The authors report their results in the treatment of 21 histologically verified cases of malignant melanoma by means of radiation, surgery, and electrosurgery. The series included 14 early melanomas which were treated by wide local excision and irradiation. Five of these patients were still alive two to six years later without recurrence. Superficial contact therapy (grenz rays) was used, the tumor dose varying between 6,000 and 8,000 r. One of the patients thus treated was alive and symptom-free two and one-half years after cessation of therapy. Of 4 whose tumors were removed by electrosurgery followed by radiotherapy, 2 were alive and well after five and six years. One of 5 patients treated with radiotherapy prior to electrocoagulation was still alive three years later. Still another, who was given radiotherapy alone, is alive and asymptomatic two years after treatment. The overall rate of survival for this group of 14 cases was between two and six years. However, among the 7 patients whose examination at the time of admission revealed metastases, only 1 was alive after two and one-half years.

The results showed that a cure is possible if the radical treatment is started while the tumor is still in an early phase of development. Heavy dosages of radiation followed by electrosurgery after three to six weeks is considered the treatment of choice in highly malignant melanoma. In all other cases, wide excision of the tumor followed by radiation therapy is recommended.

Four tables. EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Lymphosarcoma, Reticulum Cell Sarcoma and Giant Follicular Lymphoma. Long Term Results Following Radiation Therapy. J. C. Cook, K. L. Krabbenhoff, and T. Leucutia. *Am. J. Roentgenol.* 84: 656-665, October 1960. (Harper Hospital, Detroit 1, Mich.)

The authors report 514 cases of lymphosarcoma, reticulum-cell sarcoma, and giant follicular lymphoma treated from 1922 to mid 1958. The cases were staged solely on the basis of relative localization or generalization: Stage I, involvement of a single lymphatic region or two or three proximal lymphatic regions but

without symptoms of generalized disease; Stage II, involvement of two or more proximal lymphatic regions with symptoms of generalization or involvement of two or more distant lymphatic regions.

The majority of patients with Stage I disease were treated by massive technic with the administration of a tumor dose to superficial lymph nodes of 700 to 800 r at one seance. In the presence of deep node involvement, cross-firing is necessary and four or five large portals are used. Each is treated on successive days for a total tumor dose of 1,200 to 1,600 r in four to five days. Lymph node areas adjacent to known involved areas are also treated.

In Stage II cases, treatment was given to most lymph node areas. The same methods were used except that ten to fourteen large portals were treated in as many days.

The earlier cases in the series were treated at 200 kv, h.v.l. 1 mm. Cu, while more recently 250 kv, h.v.l. 3 mm. Cu, was employed. Patients with mediastinal involvement were treated either at 500 kv, h.v.l. 9 mm. Cu or 2 Mev, h.v.l. 8 mm. Pb.

Depending upon the response of the disease and the patient's condition, the treatment was usually repeated after two months with a slightly decreased dose. In exceptional cases, a third treatment series was necessary. In 41 of the cases bulky tumor masses were removed surgically prior to roentgen therapy. Nitrogen mustard was used in combination with irradiation in 22 cases.

Four hundred and two patients with lymphosarcoma and reticulum-cell sarcoma, treated between 1922 and 1954, had an absolute survival rate of 26.5 per cent. The survival in lymphosarcoma was better than in reticulum-cell sarcoma, 28.2 to 21.2 per cent. There was a preponderance of male patients. A better prognosis was shown for females, not only in absolute results but in average monthly survival of those who remained alive. The average age of patients in the entire group was 41.5 years, and the age group between twenty and fifty years had the highest absolute survival rate, 40.1 per cent. The prognosis in younger and older patients is much poorer.

Forty-three patients with giant follicular lymphoma, treated between 1936 and 1954, had an absolute five-year survival rate of 48.8 per cent.

In summary, this paper describes rapid and massive treatment of large areas of the body. Lower total-tumor doses are used and judicious repetition of treatment is advocated.

Nine tables. CAPT. HOWARD R. GOULD, M.C.
Loring AFB, Maine

Osteogenic Sarcoma in Children. Alvin B. Hayles, David C. Dahlin, and Mark B. Coventry. *J.A.M.A.* 174: 1174-1177, Oct. 29, 1960. (Mayo Clinic, Rochester, Minn.)

One hundred and twenty-nine children less than sixteen years of age with pathologically verified osteogenic sarcoma were seen at the Mayo Clinic during a fifty-year period. For 126, adequate follow-up information was available, and upon these this report is based. As previously reported, these tumors have an unusual predilection for the metaphyseal ends of long bones. In this series two-thirds of the patients had tumors arising about the knee, and 81 per cent of the lesions were in the bones of the lower extremities.

Treatment of choice in the authors' opinion is early

surgical ablation, ordinarily amputation. Note is made that two tourniquets are applied at surgery, one above the tumor and one above the proposed site of amputation, so that transection can be applied between the tourniquets and possible dissemination of tumor cells by biopsy and/or surgical manipulation minimized. Of the patients in this series, 101 of the 122 who had tumors arising at sites where amputation was considered possible were so treated. Radiotherapy has proved of limited value.

A five-year survival rate of 22 per cent and ten-year survival of 19.5 per cent are comparable to results in previously reported series and serve to emphasize the fact that these tumors are by no means hopeless. Twenty-one of 22 patients surviving five years or more had tumors so located that amputation was possible. Only one child treated by radiotherapy alone achieved a long-term survival.

One roentgenogram; 2 photomicrographs; 1 graph.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Initial Experience with Split-Dose Periodic Radiation Therapy. Paul W. Scanlon. *Am. J. Roentgenol.* 84: 632-644, October 1960. (The Mayo Clinic, Rochester, Minn.)

Over the past several years the author has evolved a system of discontinuous radiation therapy in which irregularly spaced series of treatments are separated by intervals of rest which presumably permit mitotic and metabolic recovery. This intentional departure from conventional technics of fractionated dosage was based, in part, on chance experience with 43 cases of epithelioma of the anus, 88 cases of nasopharyngeal malignant tumors, and 46 malignant processes of the palatine tonsil, in which a time analysis revealed five-year survival rates three to four times as great with broken-dose therapy as with conventional uninterrupted radiation therapy.

The results of split-dose radiation therapy in 25 far-advanced neoplasms of the neck are reported. A three-stage classification was employed: Stage I, tumors confined to the site of origin and not more than 2.5 cm. in diameter (no cases); Stage II, lesions larger than 2.5 cm. and those extending beyond the site of origin or into adjacent neighboring soft parts (3 cases); Stage III, lesions which had metastasized to regional lymph nodes or those which had involved neighboring bone or nerve tissue by invasion (22 cases).

The optimal plan of treatment is considered to be an initial three days of therapy followed by seven days of rest, another six days of therapy followed by a three-week rest period, and then another fourteen days or more of therapy in which the prescribed dose is carried to completion, usually in increments of 300 r (air). In some of the author's patients, who lived at some distance from the Clinic, a two-series treatment scheme was used.

At the time of writing, after periods of observation of from one year to three years, apparent eradication of all foci of malignancy within the fields treated had been achieved in 13 of the 25 cases. Many of the patients had received radiation therapy previously or an attempt had been made at radical surgical treatment. Several neoplasms were so far advanced clinically as to be considered hopeless from every conceivable aspect.

No attempt is made to compare the one-to-three-year arrest rate of 50 per cent with the usual five-year sur-

vival rate of 5 to 15 per cent ordinarily encountered in Stage III neoplasms of the head and neck. It is pointed out, however, that McGrath and Schmidt (*S. Clin. North America* 38: 969, 1958), in a study of 117 cases of epidermoid carcinoma of the oral cavity, found that 84 per cent of all recurrences were observed within the first twelve months and 98 per cent within two years after treatment. It is also pointed out that of 15 patients with malignant lesions not previously treated, 11 were free of disease for a year to three years after periodic therapy, a result appreciably better than would have been expected in patients with predominantly Stage III lesions after conventional continuous radiation therapy.

No complications were encountered, except the usual radiomucositis, which was found to be less severe than with continuous therapy. The patients definitely tolerated split-dose therapy much better than continuous therapy, in the same dose range, 5,000 to 6,000 r.

The author feels that these preliminary results warrant additional investigation of split-dose radiation therapy from both the research and clinical aspects. He believes that the ultimate future of this method of treatment depends upon the development of some laboratory test which will reflect the ebb and flow of mitotic and metabolic activity under the changing stresses of interrupted radiation therapy.

Examples appearing in the literature of improved results obtained with periodic chemotherapy in the treatment of lung cancer, metastatic choriocarcinoma, and retinoblastoma are cited to support the concept of split-dose irradiation.

Two tables.

DAVID L. ROBINSON, M.D.
Barksdale AFB, La.

Miniature Semiconductor Dose Rate Meter. Carl Hellmuth Hertz and Rolf Gremmelmaier. *Acta radiol.* 54: 69-80, July 1960. (University of Lund, Sweden)

The authors describe a small dose rate meter which has been constructed for measurements inside body cavities using the photoeffect in a p-n junction of a gallium arsenide (GaAs) semiconductor. The requirements for such an instrument include: small size, high sensitivity, simplicity, reliability, as well as dose rate and quality independence.

The authors' probe consists of a cylindrical GaAs crystal encased in an aluminum housing, the walls of which are 0.2 mm. thick. The GaAs crystal consists of an n-type core and a p-type-layer at the surface. The p-layer was produced by diffusing zinc atoms in the n-doped GaAs cylinder. The outer diameter of the probe element is about 2.5 mm., and its length between 10 and 25 mm. An electronic ammeter with a chopper amplifier is used. It is important to use an instrument with an input impedance as low as possible, since only in that case is a linear dependence of the photocurrent on the roentgen intensity and independence of temperature variations insured. The energy dependence is illustrated by graphs showing obvious improvements with cylindrical geometry as compared with a flat plane arrangement.

Phantom measurements are considered which include comparison of measured values with central axis depth dose data. The effect of scattered radiations, the angle of incidence of the radiation, and long-term stability are analyzed.

Eight illustrations. R. L. WIRCORSKI, M.S.
Bowman Gray School of Medicine

Depth Dose Tables for Use in Radiotherapy: A Survey Prepared by the Scientific Sub-Committee of the Hospital Physicists' Association. Brit. J. Radiol. Suppl. No. 10, 1961.

This Supplement replaces Supplement 5, of the British Journal of Radiology, *Central Axis Depth-Dose Data*. It is not, however, simply a reprinting, but an entirely new publication with revisions based on recent more accurate measurements and additions to the material. It covers a range of quality from h.v.t. (half-value thickness, suggested as a substitute for h.v.l.) 0.01 mm. Al to 31-Mv x-rays, as well as electrons from 2 to 30 Mev, field sizes from 0 to 20 × 20 cm., and F.S.D.'s from 1.5 to 100 cm., although not all combinations of these are included. In addition, tables are given showing equivalent fields of various shapes, equivalent h.v.t.'s in different materials, and a method for conversion of percentage depth doses from one F.S.D. to another and for calculation of tissue/air ratios.

LUCILLE DU SAULT
The Henry Ford Hospital

Rationalisation of Fractionation in Radiotherapy.

L. G. Lajtha, R. Oliver, and F. Ellis. Brit. J. Radiol. 33: 634-635, October 1960. (Churchill Hospital, Oxford, England)

It has been shown that for a variety of normal and malignant mammalian cells, the dose response curves are remarkably similar. In all cases the straight slope corresponding to 37 per cent of the cells surviving is of the order of 160 rads, and the shape of the survival curve is that associated with two ionizing events required in each cell "target volume" for the damage to be produced (i.e., a "two-hit" mechanism of damage is in-

volved). From this curve, calculations are made to show that by the ninth cycle following the beginning of treatment—that is, the smaller the individual fraction doses—the less efficient the depopulation of cells which results. Furthermore, it is irrelevant how the individual doses are spaced, e.g., each cycle, each second cycle, or each third cycle, the end result is the same for the same number of identical fractions.

Should, however, a "single-hit" type of dose response curve apply, the total dose may be fractionated without loss of efficiency. Consequently, if the sensitivity of the tumor cells could be rendered "single hit" type, while that of the normal tissues remained of a "two-hit" type, a significant selective radiosensitivity could be achieved.

Recent reports indicate that the dose response curve of cells which contain a nucleic acid analogue is of a "single hit" type. If the nucleic acid analogue is offered to the cells of a DNA precursor, it will be taken up only by those cells which at that time are in the process of DNA synthesis. It is likely that the proportion of cells synthesizing DNA, at a given time, would be higher in a rapidly growing population of cells than in a slowly growing one. Therefore, if a tumor grows faster than the cells in the surrounding tissue, administration of, for example, 5-bromodeoxyuridine or 5-iododeoxyuridine should result in a higher proportion of tumor cells taking up the DNA analogue than of the surrounding normal cells. In this way a higher proportion of tumor cells than of normal cells might be transformed into an "increased sensitivity (single-hit type) population."

One graph.

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RADIOISOTOPES

The Evaluation of I^{131} Therapy of Graves' Disease. Reliability and Prognostic Value of Chemical and Radioactive Iodine Studies. Jack Domnitz, H. F. Hurd, and Joseph W. Goldzieher. Arch. Int. Med. 106: 194-204, August 1960. (J. W. G., Southwest Foundation for Research and Education, San Antonio, Texas)

The interpretation of thyroid function studies following radioiodine therapy for Graves' disease has been a subject of controversy. Seventy-four cases of toxic diffuse goiter treated with a total of 92 therapeutic doses of radioiodine at Brooke General Hospital, Fort Sam Houston, Texas, were analyzed. The clinical status of the patient was considered in relation to the six-, twenty-four-, and forty-eight-hour I^{131} uptake, the protein-bound I^{131} conversion ratio, and the chemical protein-bound iodine, during periods of one through three months, four through twelve months, and thirteen months and over. An evaluation was made of the agreement and disagreement of the laboratory studies with the clinical status and the reliability and prognostic value of the laboratory test.

The following statements based on the authors' findings are made:

"1. Thyroid function studies are frequently in disagreement with the clinical status during the first year following therapy. There is greater consistency of agreement after the first post-treatment year. The twenty-four- and forty-eight-hour I^{131} uptakes are the most reliable indexes of function.

"2. When disagreement exists, the six-hour I^{131}

uptake, PBI^{131} conversion ratio, and chemical PBI tend to err on the high side, while the twenty-four- and forty-eight-hour uptakes tend to err on the low side.

"3. Prognostically, the following statements may be made: (a) Patients who become clinically euthyroid tend to remain so regardless of the laboratory findings. (b) Patients who remain clinically hyperthyroid and show hyperthyroid laboratory values are likely to require retreatment. (c) Patients who remain clinically hyperthyroid but show euthyroid laboratory values will probably become euthyroid. (d) Patients who become clinically hypothyroid and show hypothyroid laboratory values will remain hypothyroid in approximately 50 per cent of the cases.

"A significant finding is that a more rapid turnover rate of tracer I^{131} following therapy is implied by a persistently elevated ratio of the six-hour to twenty-four-hour I^{131} uptake and the persistently elevated PBI^{131} conversion ratio. The present concept of a reduced thyroidal iodine space with normal amounts of iodine handled by the gland cannot explain these changes satisfactorily when the chemical PBI concentration is considered. We suggest that the thyroiditis provoked by radioiodine—in addition to reducing the amount of functioning thyroid tissue—may also alter the function of the recovered gland substance, with production of an abnormal protein-bound iodine fraction with less potency than normal and often in increased amounts."

Seven tables.

Radioactive Iodine (I^{131}) in the Postoperative Treatment of Thyroid Cancer. William H. Blahd, Robert A. Nordyke, and Franz K. Bauer. *Cancer* 13: 745-756, July-August 1960. (VA Center, Los Angeles, Calif.)

This report summarizes the experience of the Radioisotope Service of the VA Center, Los Angeles, Calif., in the postoperative treatment of 63 cases of thyroid cancer with radioactive iodine (I^{131}) during the ten-year period from 1949 to 1959. Thirty-one of the patients received therapeutic amounts of I^{131} , and 26 of these had been followed for more than a year at the time of writing. Twenty-five patients had had total thyroidectomies, and 15 had associated radical neck dissection.

Localization of cancer metastases and postsurgical thyroid remnants was accomplished by means of the scintiscanner after patients had received large tracer doses of I^{131} preceded by thyroid-stimulating hormone (TSH) injections. I^{131} uptake was ultimately demonstrated in the lesions of two-thirds of the patients with metastases.

Individual therapeutic doses of I^{131} , averaging 100 mc and preceded by TSH injections, were administered to patients with functioning metastases. Doses were repeated at approximately four-month intervals until metastases were ablated. Smaller doses were employed to destroy postsurgical thyroid remnants.

Thyroid replacement therapy in doses sufficient to maintain the euthyroid state was prescribed after initial I^{131} therapy and between subsequent therapeutic doses.

Fifteen patients had proved metastatic lesions; 10 had demonstrable I^{131} uptake. Ten of these patients were alive at the time of the report, and 5 had lived for more than five years. Eight patients were free of demonstrable lesions. All patients who were metastasis-free after thyroid surgery were alive.

No complications of I^{131} therapy were encountered in the present series. This is attributed to the conservative dosage regimen (wherein single doses did not exceed 100 mc) and to the complete excision of normal thyroid and tumor tissue whenever possible.

The authors compare the results in their 63 patients with those in other reported series. It seems apparent that 80 per cent of patients with thyroid cancer are potential candidates for I^{131} therapy, and approximately 4 out of 5 are benefited to some extent. Considerably less than this number may be cured of the disease.

Three figures; 2 tables.

HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

Response of Pulmonary and Soft Tissue Metastases from Carcinoma of the Thyroid to Radioactive Iodine Therapy. Simon Kramer and Joseph P. Concannon. *Am. J. Roentgenol.* 84: 673-680, October 1960. (Jefferson Medical College Hospital, Philadelphia 7, Penna.)

The authors report 4 cases of carcinoma of the thyroid with soft-tissue metastases locally and metastatic disease in the lungs successfully treated with radioactive iodine (I^{131}). The series included 2 cases of alveolar adenocarcinoma, 1 of papillary adenocarcinoma, and 1 mixed papillary and alveolar. All cases showed good response to I^{131} . The roentgenographic appearance of the chest in 3 patients returned to normal, and 2 were alive and well nine years after the initial radioiodine therapy. A third was well after two years. Although there are reports of spontaneous regression and

long-term survivals in thyroid cancer, it appears significant that one of the authors' patients was almost moribund when treated and made a complete recovery.

In 3 cases ablation of the thyroid was necessary before there was uptake of I^{131} by the pulmonary metastases.

Six roentgenograms; 7 scintigrams.

PAUL MASSIE, M.D.
Quincy, Mass.

Correlation of Radioactive and Chemical Faecal Fat in Different Malabsorption Syndromes. B. D. Pimparkar, E. G. Tulsy, M. H. Kalser, and H. L. Bockus. *Brit. M. J.* 2: 894-900, Sept. 24, 1960. (Graduate School of Medicine, University of Pennsylvania, Philadelphia, Penna.)

The most accurate method of studying fat absorption from the gastrointestinal tract is the balance technique, calculating the components in ingested food and chemically determining the residue of the stools, but this is time-consuming, laborious, and expensive. The purpose of the project reported was to compare in a large series the accuracy of radioactive I^{131} -labeled triolein studies with fecal chemical intake-excretion studies as a diagnostic aid in various malabsorption syndromes. One hundred and twenty-six persons were studied: 24 normal volunteers as controls and 102 patients from the gastrointestinal service of the Graduate Hospital of the University of Pennsylvania.

In general, in about 75 per cent of those with abnormal fecal chemical fat the fecal radioactivity determination was also abnormal, while the blood-peak radioactivity was abnormal in about 50 per cent. On the other hand, of those with normal fecal chemical fat, nearly 80 per cent had normal fecal radioactivity, while the blood-peak radioactivity was normal in nearly 85 per cent. Of the two I^{131} -triolein determinations the fecal was found to be a much better index of the presence of steatorrhea than the blood-peak radioactivity test. When both studies were carried out, the index of accuracy was increased.

If, after I^{131} -triolein meals, a given patient shows normal blood peak and fecal radioactivity values, his chances of being normal are about 85 to 95 per cent, while the chances of his having steatorrhea (false negative) are about 15 to 25 per cent. On the other hand, if both values are abnormal, his chances of being normal are about 10 per cent (false positive), while the chances of his having steatorrhea are about 75 per cent.

Administration of the I^{131} -labeled triolein does not afford as adequate a quantitation of steatorrhea as does the fecal chemical balance study. If facilities for the latter test are not available, however, the triolein test (using both blood peak and fecal radioactivity determination) may be used as a diagnostic aid in the detection of steatorrhea, provided its limitations are fully appreciated.

It is recommended that, if both blood peak and fecal radioactivity are abnormal, the patient should have fecal chemical balance studies for definite establishment of the diagnosis and for the quantitative estimation of steatorrhea.

Six graphs; 8 tables.

Studies with I^{131} Triolein in South African Bantu and White Subjects, and in Patients with Myocardial Infarction. J. Metz, A. Antonis, I. Bersohn, and D. Hart. *Brit. M. J.* 2: 1270-1272, Oct. 29, 1960.

(South African Institute for Medical Research, Johannesburg, Union of South Africa)

Recent studies on the levels of blood radioactivity after the oral administration of I^{131} triolein have demonstrated significant differences between normal subjects and patients with ischemic heart disease (Seller *et al.* *Am. J. Med.* 27: 231, 1959. Abst. in *Radiology* 75: 167, 1960). While the consumption of fat and the incidence of ischemic heart disease in whites in South Africa are probably comparable to those of the people of Western Europe and the United States, the average diet of the Bantu contains little fat and myocardial infarction is rare among them.

In the present study, the absorption and plasma clearance of a test dose of I^{131} triolein was followed in 29 male Bantu and 30 white males, neither group with any evidence of disease affecting gastrointestinal absorption or of ischemic heart disease, and in 20 white males convalescing from a recent attack of myocardial infarction. All were between forty and sixty years old.

After administration of the I^{131} triolein, the mean levels of plasma radioactivity in the Bantu were lower than those of the white control group at four, six, eight, and twelve hours, but were higher at twenty-four and thirty-six hours. The mean levels of the plasma radioactivity in the ischemic heart disease patients were higher than those of the white control group throughout the thirty-six-hour period of study and higher than those of the Bantu at four, six, eight, twelve, and twenty-four hours, but lower at thirty-six hours. The mean observed peak in the Bantu was at four hours, that in the white groups was at six hours after administration of the fat load. At twenty-four and thirty-six hours after the load, the plasma radioactivity levels of the Bantu were higher than those of the white controls. This may be a further indication of faster clearance rates in the Bantu, since the higher residual levels may be due to earlier feed-back of labeled lipids.

Since ischemic heart disease is rare among the Bantu, it seems apparent that its absence may be associated with rapid fat-clearance rates and it is suggested that the disease may be partly due to an impaired rate of removal of fat from the plasma.

One graph; 2 tables.

Total Body Radiation and Dose to the Gonads from the Therapeutic Use of Iodine 131: A Survey of 20 Cases. Dorothy L. Weijer, H. E. Duggan, and D. B. Scott. *J. Canad. A. Radiologists* 11: 50-56, September 1960. (University Hospital, Edmonton, Alta., Canada)

Whole-body and gonadal radiation doses were calculated in 20 patients given therapeutic amounts of radioiodine for thyroid cancer (10 cases), hyperthyroidism (7), and ablation of the thyroid for angina pectoris (3). The method employed is illustrated in a hyperthyroid patient. It depends upon the assessment of I^{131} content in urine and feces over a five-day period and in thyroid and whole blood for a minimum of five days and up to twenty-eight days when possible. No distinction is made between rads and roentgens. It is assumed (1) that I^{131} is excreted only by the kidneys; (2) that the distribution of non-excreted extrathyroidal I^{131} is uniform; (3) that the body is homogeneous and of unit density; (4) that beta radiation is entirely absorbed within the body; (5) that differences of gonadal location do not significantly alter radiation doses from the thyroid, bladder, and colon.

The mean total-body radiation dose was 0.51 rad/mc (range 0.10-1.87 rad/mc). Lowest values were found in thyroid cancer patients with no active thyroid gland or active metastases. In non-cancer patients the mean dose was 0.67 rad/mc.

The mean dose to gonadal tissue was 0.45 rad/mc (range 0.13-1.17 rad/mc), with no significant difference between cancer and non-cancer groups. In 15 patients the largest single component of the total gonadal dose was delivered by the bladder; in 11 patients more than 50 per cent of the total came from this source. In view of the dominant role played by the bladder in gonad dose, it might be wise to increase the fluid intake of treated patients, thus encouraging frequent micturition. While this would be unlikely to hasten the excretion of I^{131} , it would reduce the resident time in the bladder.

Two graphs; 4 tables.

PHILIP M. JOHNSON, M.D.
Montclair, N. J.

Biologic Effect of Grid Cobalt 60 Radiation. John W. Lane, Walter Mauderli, and David M. Gould. *Am. J. Roentgenol.* 84: 681-686, October 1960. (J.W.L., University of Colorado Medical Center, Denver 20, Colo.)

The authors studied the comparative biologic effects of cobalt 60 with homogeneous and grid techniques, using white mice as experimental animals. The radiation source consisted of 700 curies of cobalt 60 in a Barnes-Keleket Telecobalt Therapy Unit. The source-animal distance was 50 cm. The dose rate for the homogeneous beam was 52.5 r per minute; for grid therapy 31.2 r per minute.

It was found that to cause death of 50 per cent of the animals in thirty days (LD 50/30) a larger dose was required with the use of the grid, the ratio to the homogeneous dose producing the same effect being 2.4 to 1. This figure varied, however, with the size of the dose, from 2.2 for higher doses to 2.9 for lower dosage.

The grid radiation was less effective than had been anticipated, and the volume dose had to be increased by approximately 30 per cent to yield an exposure of equal biologic effect as homogeneous radiation. This implies a relative tissue-sparing effect of the grid.

While additional data must be obtained with the use of larger animals before any final conclusion can be reached, it is suggested tentatively that, when treatment is given through a grid, doses three times those with a homogeneous beam be used clinically.

Six illustrations; 2 tables. PAUL MASSIK, M.D.
Quincy, Mass.

A Complication in Cobalt Bead Treatment of Cancer of the Bladder. Report of a Case. A. Voutilainen and O. Alfthan. *Acta radiol.* 54: 45-48, July 1960. (Helsinki University Central Hospital, Finland)

The authors report an unusual complication of cobalt bead treatment of cancer of the bladder.

Twenty-five active Co^{60} beads and 20 inactive beads, 6 mm. in diameter, were strung on a silk suture, and inserted transurethraly into the bladder as close to the tumor as possible. Five days later, when an attempt was made to remove the string of beads, it was found that the end was held up in the prostatic urethra and could not be pushed back into the bladder. With further traction, the string passed fairly easily through the pars prostatica, but the end was caught in the proximal portion of the pars cavernosa. Eight beads, which

were now outside the urethra, were removed. Roentgenography revealed a knot at the enlarged end of the string, which had evidently formed inside the bladder. Increased pulling broke the thread close to the knot, and ten active and ten inactive beads were slowly pulled out. The remaining beads were expressed by external palpation. The beads had remained in the body five hours and twenty minutes (in the urethra two hours) longer than had been calculated. It was estimated that the urethra received about 500 r and the bladder a total of 4,094 r, or 1,094 r more than originally planned. At four and a half months there was a stricture in the proximal part of the pars cavernosa, presumably due to the trauma and the radiation received during the time the beads were hung up in that region.

One roentgenogram. DAMON D. BLAKE, M.D.
Bowman Gray School of Medicine

Preferential Uptake of Phosphate by Premalignant and Malignant Lesions of the Vulva. Donald G. C. Clark, Barnett Zumoff, Alexander Brunschwig, and Leon Hellman. *Cancer* 13: 775-779, July-August 1960. (Memorial Center for Cancer and Allied Diseases, New York, N. Y.)

The uptake of intravenously administered radioactive phosphorus (P^{32})-labeled sodium phosphate was studied in 13 patients with a variety of vulvar lesions. In areas of inflammation and radionecrosis, the uptake was not significantly above the normal range. Precancerous lesions (kraurosis and leukoplakia) took up 1.5 to 2.4 times as much P^{32} as did normal tissue. Carcinoma *in situ* took up 1.9 to 3.0 times and invasive cancer 2.4 to 6.9 times the normal mean. Thus, there was a gradation of preferential uptake corresponding to the presumed stages in the development of invasive cancer. The differential uptake between normal tissue and premalignant and malignant lesions was sufficiently great to be of diagnostic value. Those tissues whose uptake was more than 1.6 times the mean uptake of comparable normal tissue were invariably precancerous or cancerous; lesions whose uptake was more than 2.4 times the normal were invariably malignant. Vulvar lichen sclerosus et atrophicus behaved like a precancerous lesion, in terms of radiophosphorus uptake.

Three figures; 1 table.

HAROLD A. SWANSON, M.D.
Calgary General Hospital, Calgary, Alta.

Effect of X Rays on the Uptake of Phosphorus 32 by the Mouse Knee Joint. Dependence upon the Spacing Interval of the Effect Produced by Two Spaced Equal Dose Fractions. C. W. Wilson. *Brit. J. Radiol.* 33: 636-639, October 1960. (Westminster Hospital, London, S.W. 1, England)

The author reported in a previous paper (*Brit. J. Radiol.* 32: 547, 1959) that if depression of P^{32} uptake by the mouse knee joint is used as the measure of biological effect produced by a dose of 2,000 r of x-rays, the effect produced when the dose is given at once is considerably greater than it is if the dose is given in two equal 1,000 r fractions spaced with an interval of either one or four weeks. In both instances effect of the second fraction was much less than that of the first. The results of experiments designed to study the effect of spacing intervals between the fractions of less than and longer than one week are now presented.

Three-week-old male albino mice of a closely inbred strain were given 2,000 r to the left hind leg in a single

session and $2 \times 1,000$ r to the right hind leg, with intervals between fractions ranging from one hour to two weeks. Four to six weeks after the second irradiation, when the effect of irradiation upon uptake of P^{32} is maximal and constant, the isotope in saline was injected intraperitoneally (0.4 μ g./gm. body weight). One to two hours after injection, when uptake was maximal, the animals were killed and the P^{32} uptake measured. The ratio of specific uptake of the left knee joint to that of the right knee joint decreased steadily for a period of approximately five hours; thereafter, for an interval of at least two weeks, it remained constant. Calculations based on previous work show that this constant value is not significantly different from that to be expected if the second 1,000 r had no effect. Therefore, one must conclude, as before, that some effect is produced by the second 1,000 r dose but that this is only a small portion of the full effect that the same dose produces in a normal unirradiated knee joint.

An attempt is made to explain the results with a view to emphasizing the dynamic character of the events that may follow irradiation of a complex tissue.

Two graphs; 1 table. LUCILLE DU SAULT
The Henry Ford Hospital

Malignant Effusions Treated by Colloidal Radioactive Yttrium Silicate. J. Walter. *Brit. M. J.* 2: 1282-1284, Oct. 29, 1960. (University of Sheffield, Sheffield, England)

In a search for an alternative to radioactive gold for control of malignant pleural and peritoneal effusions, a preliminary trial was made of a new compound, colloidal radioactive yttrium silicate ($Y^{90}_2(SiO_3)_3$) in 15 cases. Since some of the patients were in poor condition with a bad prognosis because of the extent of the growth, it is not surprising that out of the 15 treated, 6 died within a month. In 6 of the 9 remaining cases, useful palliation was achieved for periods ranging from five to nineteen months. This number is small, but the results compare favorably with those reported for Au^{198} . The quantities injected ranged from 21 to 75 mc. Samples of blood and cavity fluid were withdrawn at intervals, so far as the patient's condition permitted; urine was assayed in daily batches; and a body scan was made after twenty-four hours.

Distribution was almost always satisfactory; 1 case of loculation was found. General reactions were minimal and there was no obvious effect on the blood count. Blood and urine levels never gave cause for anxiety. Serial assays of cavity fluid showed that in 9 out of 12 cases precipitation was quite marked and quite rapid, as judged by the concentration of activity in the fluid. After the first day the fall of activity in the fluid was only gradual.

The advantages of yttrium over gold are discussed, especially the superior surface penetration of the beta particles and the lesser radiation hazards owing to the absence of penetrating gamma radiation.

One diagram; 2 tables.

The Effect of Experimental Cerebral Concussion on the Blood Volume and the Pattern of Distribution of Radioactive Chromium-51 Tagged Red Blood Cells. Edmund A. Smolik and Francis P. Nash. *J. Neurosurg.* 17: 669-676, July 1960. (St. Louis University School of Medicine, St. Louis, Mo.)

Blood-volume studies, hematocrit determinations, and abdominal-scanning profiles were carried out with

chromium-51 tagged red blood cells in 16 dogs in which concussion had been produced. Six normal dogs served as controls. In the control group a uniform and reproducible pattern of chromium-51 tagged red blood cells was obtained both volumetrically and by a visceral scanning profile. Of 10 dogs surviving concussion, 9

exhibited significant changes in blood volume and in distribution of cells. These experiments show that in animals with experimentally produced concussion there is an immediate vasoconstriction, followed by a plasma dilution of the remaining cell mass.

Five illustrations.

RADIATION EFFECTS

Osteogenic Sarcoma of the Skull Following Roentgen-Ray Therapy for Benign Pituitary Tumor. John M. Meredith, F. B. Mandeville, and Saul Kay. *J. Neurosurg.* 17: 792-799, July 1960. (Medical College of Virginia, Richmond, Va.)

The case is reported of a middle-aged woman in whom an osteogenic sarcoma of the skull developed approximately six years after the administration of roentgen therapy for a benign lesion of the pituitary (chromophobe adenoma). The four criteria set forth in the literature for the diagnosis of postirradiation osteogenic sarcoma are believed to be fulfilled in this case: (1) roentgenographic evidence of a normal vault of the skull before the irradiation; (2) development of the sarcoma in the area included within the radiotherapeutic beam; (3) a relatively long symptom-free latent period (six years); (4) histologic proof of sarcoma in the previously normal bone. It is emphasized that adult-type osteogenic sarcoma of the skull, whether of the rare postirradiation type or of spontaneous origin, is very unusual; in middle-aged persons free of Paget's disease, as the authors' patient, it occurs much more frequently in *extracranial* bones, e.g., in the extremities or spinal-pelvic axis.

The authors stress the importance of irradiating intracranial structures or neoplasms only when such therapy seems definitely or strongly indicated, as there always appears to be at least a potential danger of osteogenic sarcoma developing in the overlying skull when such roentgen therapy is given.

Five illustrations.

X-Ray Diagnosis of Radiation Injuries of the Lung. H. Lichtenstein. *Dis. of Chest* 38: 294-297, September 1960. (Workers Sick-Fund, Haifa, Israel)

The author describes the roentgen findings in 50 patients with radiation injuries of the lung following postoperative x-ray therapy for carcinoma of the breast. The age range was from thirty-two to seventy-one years, with only 5 women under forty. The relatively young patients eventually suffered the most severe damage. In 20 of the 50 cases (40 per cent), the injury was detectable only on roentgen examination. When symptoms did occur, the most outstanding were dyspnea (13 cases), cough and sputum (11), and chest pain (6).

Two stages in the process of radiation damage are recognizable both histologically and roentgenologically. The early reaction is of an exudative character, the so-called radiation pneumonitis. This is followed by radiation fibrosis, the second stage. During the acute inflammation, a homogeneous shadow is seen in the irradiated area, chiefly in the infraclavicular portion of the lung; this was observed in 44 of the author's 50 cases. In the fibrotic stage, roentgenography shows ribbon-like shadows, clearly defined, connecting the hilus and the periphery of the lung. Radiation injuries are never demonstrable on the roentgenogram until at least one month after the treatment.

In the differential diagnosis two points are stressed: (1) The localization of the lesions is in the anterior layers, which are most exposed to the x-rays during irradiation. This is particularly important in the differentiation from tuberculosis. (2) Tomography reveals dense shadows with numerous bright hole-like spots, representing the enlargement of medium-sized and small bronchi.

Of 27 patients in the present series who suffered severe injuries, 16 did not exhibit evidence of resorption, and a heavily scarred tissue took the place of the primary lesion. In 11 patients the damage appeared at first to be irreversible, but during further observation the signs of resorption became quite remarkable.

Cortisone was administered in 6 cases of severe pneumonitis, but roentgen findings showed no changes attributable to this treatment.

Four roentgenograms; 2 tables.

JOHN P. FOTOPoulos, M.D.
Northwestern University Medical School

The Functional Effect of Pulmonary Irradiation. Maurice Sutton. *Brit. M. J.* 2: 838-841, Sept. 17, 1960. (Hammersmith Hospital, London, England)

Serial lung function studies were performed before, during, and after pulmonary irradiation for carcinoma of the breast or carcinoma of the lung. Radiotherapy was administered with either a conventional 240-kv deep x-ray machine or with an 8-Mev linear accelerator. Dosages delivered were those in general usage for cancer of the bronchus or of carcinoma of the breast pre- or postoperative. Three measurements were made at each patient visit: vital capacity, indirect maximum breathing capacity, and standardized ventilation. Only those patients capable of performing these three function tests satisfactorily were accepted for the analysis.

Of 146 patients with histologically proved carcinoma of the bronchus, treated with the 8-Mev accelerator, 42 were alive at the end of twelve months; 28 had serial lung function studies at monthly intervals, while 14 were incapable of performing the tests. Ten patients with bronchial carcinoma received a radical course of conventional radiotherapy; all but 2 died between the fifth and twelfth months after treatment. An unstated number of patients undergoing radiotherapy for carcinoma of the breast were also studied.

At about the third week of treatment with the 240-kv apparatus, patients tended to show a falling off in lung function. This coincided with the skin reaction and general malaise. Patients treated with the 8-Mev linear accelerator do not experience skin reaction and have much less general discomfort; as a reflection of this they continue to improve from the functional point of view. In both groups continued mild improvement in lung function is observed for a variable time after therapy, followed by a period in which it remains constant. It deteriorates suddenly beginning about two

months before death. The author believes that the depression in pulmonary function seen in patients receiving 240-kv radiotherapy is probably attributable to the difference in radiation reaction.

After periods of one year, in patients surviving in fair general condition, a moderate functional disability usually results from direct pulmonary irradiation by supervoltage x-rays. All these patients show some evidence of post-irradiation pulmonary fibrosis.

No real functional disability results from radiotherapy for carcinoma of breast when modern technics (glancing beams) are employed.

Four graphs.

JAMES W. BARBER, M.D.
Cheyenne, Wyo.

Spontaneous Femoral Neck Fracture Following Pelvic Irradiation. Report of Three Cases. Jerome G. Finder and Melvin Post. *Arch. Surg.* 81: 545-552, October 1960. (111 N. Wabash Ave., Chicago 2, Ill.)

Three cases of spontaneous femoral neck fracture following irradiation to the pelvis are reported. Trauma was not an etiologic factor in these cases. Two of the patients had been treated by radium and roentgen therapy for squamous-cell carcinoma of the cervix; the fractures appeared about two years later. In both cases good results were obtained with autogenous bone grafts, supplemented by internal fixation with a Smith-Petersen nail. The third patient received about 2,100 r to the pelvis following removal of a papillary cystadenocarcinoma of the ovary. About eighteen months later there was an acute onset of pain in the left hip and thigh, and a subcapital fracture was discovered. This was attributed to metastasis, and further irradiation (1,800 r) was administered. Subsequently roentgenograms revealed a healed fracture with varus deformity. At the time of the report the patient had a 1/2 inch shortening of the left leg, and a flexion contracture of 15° had developed, with increasing disability. A subtrochanteric osteotomy was recommended but had not been performed.

The possibility of fracture should be suspected in every patient who has received irradiation for pelvic cancer in whom signs and symptoms referable to the hip occur.

Ten roentgenograms.

Osteoradionecrosis in the Region of the Hip Joint. Wilhelm Oelssner, Joachim Pfeiffer, and Helmut Buttenberg. *Strahlentherapie* 109: 200-210, June-July 1959. (In German) (Universitäts-Röntgeninstitut Leipzig, Germany)

This report is based on 25 cases of radionecrosis of the hip joint which developed in a series of 909 patients following treatment of gynecological cancer by irradiation between 1952 and 1958.

The treatment factors were: 180 kv, h.v.l. 0.95 mm. Cu, 3 anterior ports, 3 posterior ports, 1 gluteal and 1 sacral field. The maximum skin dose varied from 3,000 to 3,800 r (depth dosages are not stated). In some instances a supplementary perineal port was used. The osteoradionecrosis was of four types: (1) trabecular changes of the neck of the femur, (2) fracture of the femoral neck, (3) aseptic necrosis of the femoral head, and (4) necrosis of the acetabulum with or without protrusion into the pelvis. Symptoms and differential diagnosis are discussed, with citation of illustrative cases.

The first description of a case of osteoradionecrosis of

the femoral neck was published by Baensch in 1927; up to the year 1950, 150 such cases have been reported. The frequency with which the bony changes develop has been variously stated as between 1.0 and 2.75 per cent of the cases of gynecological cancer treated by radiation therapy. The symptoms deriving from the occurrence of the bony changes, such as sciatic pain and soreness around the hip joint, have manifested themselves as early as three months and as late as thirty-one months after therapy, the average interval being thirteen months. The damage suffered by the osteocytes and small capillaries is mainly attributable to absorption of the high energy radiation employed and inadequate protection of the hip joint during application of an adequate dose to the parametrium. No correlation was observed between the patient's weight, age, or constitution and the occurrence of osteonecrosis.

Bed rest and vitamin D and calcium preparations proved beneficial in treating the bony changes. Cases of complete fractures and transformation zones that did not respond to conservative therapy were handled surgically (e.g., nail fixation) to prevent the possible development of a painful pseudarthrosis.

Seventeen roentgenograms.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Determination of the Ovary Dose in Diagnostic Roentgen Procedures. Finn Devik, Jon Flatby, and Leiv Berteig. *Acta radiol.* 54: 296-304, October 1960. (Rikshospitalet, Oslo, Norway)

The estimation of the dose received by the ovary during diagnostic roentgen procedures by direct measurements in postmortem material and in a phantom and by indirect measurements in the living is discussed. The authors conclude that the practical determination of the gonad dose in women must be accomplished by indirect measurements. Acceptable values for the ovary dose may be obtained by a special technic of *in situ* measurements in the rectum supplemented by phantom measurements. It is assumed that for certain examinations the number of clinical measurements may be reduced in favor of phantom measurements. The phantom moreover permits an estimation of the correcting factor of the measured rectal dose and the true ovary dose. In most cases, however, with the technic employed, this factor does not seem to vary greatly. The importance of the employment of the phantom as a reference standard is emphasized.

The construction of the phantom is described.

Five figures, including 1 roentgenogram; 1 table.

Isodose Curves About the Beds of Patients Containing Intracavitary Radium or Cobalt 60 Sources. William F. Barry, Jr., and Ronald Krueger. *Am. J. Roentgenol.* 84: 712-714, October 1960. (Duke University Medical Center, Durham, N. C.)

The authors measured the dose delivered by intrauterine or vaginal radium or radioactive cobalt at various points outside the patient's body, namely, at the head and foot of the bed and at either side, 4.3 cm. above the sternum, and 4.3 cm. above the symphysis pubis. The highest dose was found at the pubis, the maximum being 2,500 mr/hr. and the minimum 1,000 mr/hr. Even with the smaller dose it would be possible for a nurse, in the course of irrigating a catheter, adjusting binders, etc., to receive the weekly permissible maximum dose to the hands in ninety minutes.

As a result of their observations, the authors offer a series of recommendations, which are essentially: Stay as far away as possible and, in the case of visitors, spend as little time as possible with the patient. Pregnant women should stay away altogether.

Two isodose charts; 1 graph.

PAUL MASSIK, M.D.
Quincy, Mass.

Radiation Accidents. Eugene L. Saenger. *Am. J. Roentgenol.* **84**: 715-728, October 1960. (Cincinnati General Hospital, Cincinnati 29, Ohio)

The author reviews the literature dealing with radiation accidents, which he defines as "unforeseen occurrences, either actual or suspected, involving exposure to, and contamination on or within, humans and the environment by radiation... in a short time period of seconds to days." Chronic occupational or long-term exposures are not considered in this paper.

The two basic types of radiation accident are (1) exposure to an external source, and (2) contamination on or within the body by radioactive materials. In most radiation accidents, there is a history of significant human mistakes often contributing to the accident and impeding its handling. Once the exposure has occurred, many persons are thrown into panic and behave most irrationally. It is with this thought in mind that the author presents a simple emergency plan to be followed in the event of a radiation accident.

One of the problems in the acute radiation syndrome is the calculation of the dose to which the individual has been exposed or has absorbed. Film badges and personnel dosimeters may be too sensitive for the dose involved in an accident. Dosimetry is a technically difficult problem and usually requires days to weeks before calculations are available. Since physical data are often not available, in order to assign exposed patients to dose groups it is necessary to correlate the clinical manifestations and laboratory data in an attempt to foretell the course.

The acute radiation syndrome is divided into four stages: (1) the initial or prodromal stage (eight to forty-eight hours duration); (2) the latent stage (two to three weeks); (3) manifest illness stage (two or three to six weeks); (4) recovery stage (eight to fifteen weeks). Five clinical radiation injury groups are recognized. In Group I the patients are mostly asymptomatic, with occasional prodromal symptoms. Group II shows a mild form of acute radiation syndrome, with moderate laboratory and clinical evidence of hematopoietic derangement. Group III is characterized by a serious course, with severe hematopoietic complications and some evidence of gastroenteric damage. Group IV is an "accelerated version" of acute radiation syndrome, with gastroenteric involvement dominating the clinical picture. Group V follows a fulminating course, with marked central nervous system impairment. The usual doses necessary to cause each degree of injury are given, and many helpful hints about the early grouping of patients are included. Laboratory studies are taken up in considerable detail, and the therapeutic measures for each group are outlined. For the recommended measures the original paper should be consulted. Use of chelating agents is discussed, with indications and contraindications.

Five figures; 7 tables.

CAPT. HOWARD R. GOULD, M.C.
Loring AFB, Maine

Large Volume Irradiation, Immunity Response and Bone Marrow Replacement: A Symposium. *Brit. J. Radiol.* **33**: 577-592, September 1960.

At the Annual Congress of the British Institute of Radiology, Dec. 11, 1959, a symposium was presented on large volume irradiation, immunity response, and bone-marrow replacement. Abstracts of the four contributions follow.

I. The Application of Stored Autologous Bone Marrow in the Treatment of Advanced Malignant Disease.

(A) Clinical Aspects. K. A. Newton. (B) Hematological Aspects. J. G. Humble. *Brit. J. Radiol.* **33**: 577-581, September 1960. (Westminster Hospital, London, S.W. 1, England)

After discussing the relative merits of the intravenous injection of the patient's own stored marrow or of marrow which is aspirated on completion of irradiation from an unirradiated site, Newton cites some of his clinical experience with the procedures. He favors pre-treatment aspiration of bone marrow.

Seven patients with multiple pulmonary metastases were treated through 25 × 30 cm. anterior and posterior ports with the 2 Mev Van de Graaff generator. Marrow injection brought about repopulation of the marrow spaces and appeared to satisfactorily overcome the hematological complications in 5 of the patients. Radiation pneumonitis, however, proved to be a problem. Daily doses of 150 r to a total dose of 2,500 to 2,750 r were found to be the upper safe limits. Beyond this, pneumonitis could not be avoided and was the cause of death in 3 patients. Macroscopic evidence of disease was eliminated in 6 patients.

A number of patients with malignant melanoma were given marrow injections after large dose chemotherapy, Degranol (a mannitol mustard) in several patients and nitrogen mustard in others. Results were not impressive, and it is suggested that massive chemotherapy would be more useful in advanced neoplasms of radio- and chemotherapeutically sensitive type, such as lymphoma, testicular seminoma, and oat-cell carcinoma of the bronchus.

Humble's paper consists of a short restatement of the experiences related by Newton.

In each patient red-marrow aspirations were made from the sternum and the anterior and especially the posterior iliac crests. Sieving and centrifuging removed the fat present, and the preparation was stored in ampules at 79° C. in 15 per cent glycerol. When patient treatment was completed, the ampules were quickly thawed and the material slowly injected intravenously. Too rapid injection produced a chill and hemoglobinuria in 1 patient.

Of 7 patients treated with large volume, high-dose radiotherapy, rapid regrowth of sternal bone marrow was obtained in 5. Of 7 patients receiving massive chemotherapy (5 for multiple metastases of malignant melanoma, 1 for carcinoma of the esophagus with widespread metastases, 1 for Hodgkin's disease), 2 showed apparent complete restoration of marrow function. What is described as a tremendous degree of regeneration of the marrow in the shaft of the humerus was found in 1 case.

It is hoped that by the use of such technics, better clinical remissions in advanced disseminated malignant disease may be obtained.

Two graphs.

DON E. MATTHIASEN, M.D.
Phoenix, Ariz.

II. Immunological Studies of Mouse Radiation Chimeras. D. W. H. Barnes. *Brit. J. Radiol.* **33**: 582-585, September 1960. (Radiobiological Research Unit, Harwell, Berks., England)

By giving properly adjusted doses of whole-body irradiation the immunological response of a mouse may be permanently inactivated, and it must then depend upon marrow inoculations for its subsequent immunological activities. In *isologous* chimeras the injected hematopoietic tissues are from mice of the same strain. *Homologous* chimeras receive injections from different strains. When injections are made between species (rat to mouse) the chimeras are called *heterologous*.

Skin homografts survive longer in isologous chimeras than in unirradiated mice, survival time being partly dependent on the cell type—spleen, fetal liver, or bone marrow—which has been injected. Also, isologous chimeras survive longer than the homologous and heterologous, unless larger doses of homologous, or larger still of heterologous cells are given. Death of the mice is not clearly explainable immunologically, but the author believes that it is due to reaction resulting from sensitization of tissue derived from the donated cells against the antigens of the host. This secondary or homologous disease can be avoided by choosing antigenically compatible but unrelated donors. In homologous and heterologous chimeras, secondary disease causes a high mortality but usually some animals survive. In these it is thought that the rat cells have become immunologically inert with regard to the host or that mouse lymphoid cells, when they reappear in the presence of rat antigens, might be tolerant of them.

In any event, that the host can become tolerant of the graft raises the hope that it may become possible with radiation and bone-marrow transplantations to achieve organ grafting from the same donor.

One table. DON E. MATTHIEN, M.D.
Phoenix, Ariz.

III. Lymphoid Tissue Replacement. H. E. M. Kay. *Brit. J. Radiol.* **33**: 585-587, September 1960. (Royal Marsden Hospital, London, S.W. 3, England)

It has been calculated that the total volume of lymphoid tissue in a healthy adult is around 300 to 1,000 grams. Following lymphoid tissue destruction by surgery or irradiation, restoration of the lymphoid system and its activities appears to require the replacement of appropriate reticuloendothelial stem cells.

Among other defense functions, lymphoid cells appear to exert a suppressive effect on lymphosarcomatous cells in mouse lymphosarcoma. Ideally, after irradiation, recovery should be assisted by bone marrow, gamma globulin, antibiotics, and lymphoid cells. However, ordinary adult lymphoid cells are almost sure to react against their new host with fatal effect.

The fetus and newborn animal have a tolerance for foreign cells, probably because they present an environment in which no cells are capable of a primary antibody response. Studies in this connection suggest that in the future it may become possible to induce artificial tolerance in the cells which are to be injected.

Lymph-node transplants in agammaglobulinemia have been tried without lasting benefit. Injections of fetal liver cells, fetal spleen, thymus and lymph nodes have been tried in agammaglobulinemia, also with unpromising negative results. The author expresses the hope, however, that before long it will be possible to

make tolerant grafts, so that the lymphopenic patient may be treated, and the scope of intensive radiotherapy will thereby be enlarged. DON E. MATTHIEN, M.D.
Phoenix, Ariz.

IV. Consideration of the Theory of Bone Marrow Grafting as Treatment of Radiation Damage. L. G. Lajtha. *Brit. J. Radiol.* **33**: 588-592, September 1960. (Churchill Hospital, Oxford, England)

This paper is presented to show that, aside from practical difficulties, there may not be good theoretical reasons for marrow grafting in combating radiation damage in man.

First, the point is made that while the bone marrow is a markedly radiosensitive organ, there is no good evidence that bone marrow cells are more radiosensitive—in terms of reproductive integrity—than other cells. Experiments are cited that show that, in this respect at least, all mammalian cells have a very similar degree of sensitivity.

Second, bone-marrow is called a sensitive organ because the damaged proportion of its cell population dies off faster than can be compensated for by the stem cells, which divide on specific demand, governed by homeostatic factors.

Third, as bone marrow cells have a relatively short life span, it is the donated stem cells which are responsible for the growth of the graft. A dose of 700 rads, which causes bone-marrow death, destroys less than 98 per cent of stem cells, and bone marrow will recover with as little as 1 per cent of the normal stem cells present. After a dose of 500 rads, about 10 per cent of stem cells remain intact; in this case marrow grafting adds only about 1 per cent to the existing 10 per cent, which is unlikely to be of much significance.

Generally speaking, if sufficient irradiation is received to prevent marrow recovery, then the intestinal epithelium does not recover either, and in spite of successful marrow grafting, an "intestinal death" will follow. With smaller doses, more marrow stem cells would be left intact than could reasonably be given by grafting.

Since radiosensitivity, with respect to ability to reproduce, is about the same for malignant cells and normal cells, attempts to destroy all malignant cells in leukemia by whole-body irradiation are doomed to failure. There is no tumor sterilizing single dose of total-body radiation, which, even in the presence of successful marrow grafting, will not kill the patient.

In partial-body irradiation, more autologous marrow will be protected than could reasonably be given by autografting.

The same limitations generally apply to chemotherapy. There is no evidence that any of the existing chemotherapeutic agents are tumor-specific; and bone-marrow damage is the chief limitation in tumor therapy.

The author concludes with the suggestion that, instead of marrow grafting, careful substitution therapy with sterile nursing, antibiotics, and frequent platelet transfusions may avert death until the regenerating marrow can take over. Further, marrow stimulation by anoxia and white cell depletion could be accomplished by means of massive venesection after irradiation. Theoretically, this should stimulate regeneration of all the marrow elements, and animal experiments could easily furnish the proof.

Three figures. DON E. MATTHIEN, M.D.
Phoenix, Ariz.

The Differences in Response of Grafted and Normal Skin to Ionizing Irradiation. Clinical Observations. Philip Rubin and Jerry W. Grise. *Am. J. Roentgenol.* 84: 645-655, October 1960. (Strong Memorial Hospital, Rochester 20, N. Y.)

With the advent of more radical surgical procedures for cancer, reconstructive surgery and postoperative irradiation of graft sites are increasing. The authors present a series of 7 cases in which radiation was given through a grafted area. Four patients had undergone mastectomy, 2 had head or neck cancer, and in 1 the graft was in the popliteal area. Several general conclusions about differences in response of grafts and normal skin to irradiation were reached.

1. A graft older than one year is more radioresistant than normal skin. In the 3 cases in this category, the usual initial response, such as erythema and desquamation, was not seen in the graft. In 1 of the patients, however, late necrosis developed three or four months after irradiation. This case was quite complicated in that back-to-back skin and buccal mucosa grafts were involved.

2. Fresh grafts (up to three months) react earlier and more vigorously than normal skin. There were 3 cases, all postmastectomy, in this group.

3. Recovery phenomena are delayed in fresh grafts and absent in old grafts. Healing of ulcers in fresh grafts takes longer than in normal skin. In the old graft cited above, with late necrosis, healing did not occur.

4. Similarity in tolerance of normal and grafted skin occurs during the transitional phase (three months to one year). One case (popliteal area) was included in this group, and the reactions on graft and normal skin were identical.

The authors feel that graft tolerance is not a serious complication in the course of therapy, since, except for the case of late necrosis, all of the grafted sites recovered slowly but completely.

Twelve figures. CAPT. HOWARD R. GOULD, M.C.
Loring AFB, Maine

Radiation Protection of Fish Effected by Exposure to Low Temperatures. Charles-Marie Gros, Roger Keiling, and Jacques Bloch. *Strahlentherapie* 109: 241-245, June-July 1959. (In German) (Chaire d'électroradiologie de la Faculté de médecine de Strasbourg, France)

Immersion of fish (*Carassius Carassius L.*), irradiated with doses up to 15,000 r, and their maintenance in water kept at low temperature markedly increased the survival rate as compared to that of irradiated controls replaced in water at normal temperature (18° C.). Fish of the particular species employed were selected as particularly appropriate for this study because of their small size (10 cm. long; average weight, 12 gm.) and their ability to keep alive for about one hour outside the water. They were subjected to the irradiation during this interval. Up to that moment, they were kept in a large aquarium, maintained at normal temperature. Immediately following irradiation, the fish (some 700 of them) were distributed among a number of small aquariums, maintained respectively at temperatures of 25°, 18°, 13°, 7° and 3° C. These temperatures remained constant throughout the observation period of about two months. Irradiation was effected at 200 kv, with a 3-mm. Al filter and a focal distance of 14 cm.

For the fish which had been immersed in water at 18° the LD 50 was approximately 1,800 r. There was general survival after a dose of 400 r, and no survival after a dose of 7,500 r. With immersion at 25°, all fish irradiated with a dose of 2,000 r died within eight days. It thus appeared that exposure to the higher temperature increased the lethal effect of irradiation.

By contrast, immersion in water at 7° after a dose of 2,000 r was followed by survival of all the fish for eight days. With the temperature of the water at 3°, 60 per cent survived for two months after having received a radiation dose of 5,000 r. All fish died within twenty-four days when they were placed in water at 18° after having received the same dose. Post-irradiation immersion in water of low temperature thus markedly increased the survival rate. The protective or sparing effect is probably a consequence of the lowered basal metabolism induced by the cold water.

The authors also observed that the larger irradiation doses protected the fish to some extent against the effects of exposure to low temperatures. Thus, the survival of the fish immersed in water at 3° was greater after doses of 4,000 and 5,000 r than after 3,000 r. When, at the end of the observation period of fifty days, the irradiated fish as well as nonirradiated controls were placed in water at 15°, the irradiated fish promptly died. At this temperature, the protection against radiation damage afforded by the lower temperatures was, therefore, no longer available.

Seven tables. EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Genetics of Human Cell Lines. III. Incorporation of 5-Bromo- and 5-Iododeoxyuridine into the Deoxyribonucleic Acid of Human Cells and Its Effect on Radiation Sensitivity. B. Djordjevic and Wacław Szybalski. *J. Exper. Med.* 112: 509-531, Sept. 1, 1960. (Institute of Microbiology, Rutgers University, New Brunswick, N. J.)

Strain D98S, a single cell isolate derived from human sternal marrow, can be cultivated indefinitely in the presence of 3×10^{-6} M 5-bromodeoxyuridine (BUDR) without loss of cell viability. During this time, BUDR is incorporated into both strands of the DNA molecules, replacing up to 45 per cent of the thymidine and thereby rendering the cells highly sensitive to ultraviolet light and to x-rays. Several aspects of the incorporation of BUDR and another thymidine analogue, 5-iododeoxyuridine (IUDR), including its effect on radiosensitivity, were the subjects of this study. The opportunities afforded by BUDR labeling of DNA synthesized under various conditions were exploited, and the physicochemical and biological properties of such modified DNA were evaluated.

Cells grown for a limited period of time in the presence of IUDR become ultraviolet-ray-sensitized, while prolonged cultivation with IUDR results in the loss of cell viability. Preliminary experiments indicated that BUDR incorporation significantly increases the sensitivity of D98S cells to x-rays. The "one-hit" dose (about 37 per cent survival) of approximately 270 r for the control cells was reduced to 125 or 76 r for cells cultivated for two days in the presence of 10 or 59 μ g. BUDR per milliliter respectively. The properties of the BUDR label permitted the demonstration that: (a) human DNA replicates in a "semiconservative" manner; (b) the degree of radiosensitization of BUDR-treated cells depends on whether the DNA has been

substituted in one strand only ("unifilarly") or in both strands ("bifilarly"); (c) functional human DNA is produced during partial inhibition of protein synthesis. The potential applicability of this new rational principle of radiosensitization to the radiotherapy of neoplastic diseases is discussed.

Seven figures; 7 tables.

The Problem of Screening Beta Rays. T. Musialowicz and F. Wachsmann. *Atompraxis* 6: 404-407, October-November 1950. (In German) (Institut für Strahlenkunde der Universität Erlangen, Germany)

Shielding against beta rays is important since the dose of absorbed radiation is usually very high. Protection of the eyes is of special significance since they are five times more radiosensitive than the skin of the face. Eyes as well as testicles need protective shielding.

One of the questions involved in shielding beta rays is the amount of x-radiation produced in the cover film. Since the proportion of x-rays produced in the absorber increases with its atomic number, there was doubt as to the purposefulness of using lenses with a higher effective atomic number in safety goggles for protection. Calculations and empirical measurements both showed that the atomic number of the shielding material makes no difference, since even with lead the proportion of x-rays is less than 0.1 per cent.

Three graphs; 2 tables.

Hematologic Changes Associated with Radiation Sickness. Z. Dienstbier, M. Arient, and J. Pospišil. *Atompraxis* 6: 416-421, October-November 1960. (In German) (Biophysikalisches Institut, Karls-Universität, Prague, Czechoslovakia)

Radiation sickness can be a serious complication of

radiotherapy, and it is therefore desirable to predict its occurrence with the aid of specific hematologic changes. The authors believe that characteristic reactions exist. In this article the blood changes following a single roentgen-ray exposure are discussed.

Rats were given a single dose of 700 r of roentgen rays. Within twenty-four hours there was always neutrophilia, eosinopenia, and lymphopenia. Only the lymphopenia can be considered specific as it is independent of adrenal action. All acute hematologic changes can be altered by means of adrenalectomy, with the exception of the lymphopenic reaction. The latter can always be found within twenty-four hours following radiation exposure.

The degree of lymphopenia depends on the size of the irradiated field. To prove this point the authors applied partial body irradiation. Four groups of rats were given 25 r, 100 r, 600 r, and 1,000 r, respectively, and the blood was tested four, eight, and twenty-four hours afterward. The greater the field, the more pronounced was the induced lymphopenia. Similar reactions can also be found in mice, rabbits, and dogs. The degree of lymphopenia can be determined one hour after the irradiation regardless of the applied dose.

Neutrophilia as well as the subsequent leukocytosis and eosinophilia follow the initial leukopenia. Their course fails to show any correlation with the absorbed radiation dose and is considered a nonspecific reaction secondary to tissue damage. The induced lymphopenia, however, remains constant following the initial postirradiation period. Its quantitative determination is important in judging the severity and course of radiation sickness.

Five tables; 8 curves.

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Northport, N. Y.

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